Pd-C. The mixture was filtered using Celite and the filtrate was evaporated to dryness. The white crystalline solid was recrystallized from 6 ml of H_2O to give 0.36 g (7.3% overall yield from **10**) of **12** hemihydrate: $[\alpha]^{26}D$ −103° (*c* 1.1, DMF) [lit.[11] (for the D enantiomer) $[\alpha]^{26}D$ +102.4° (*c* 0.99, DMF)]; uv max (pH 1) 253 mμ (ε 12,700) and 274 sh (8800), (pH 11) 258–265 mμ (br, ε 12,000), (MeOH) 253 mμ (ε 14,500); nmr (DMSO-d_6–D_2O) δ 6.13 ("q," 1, $J_{1'-2',2''}$ = 3.5 and 7.5 Hz, H_1'), (DMSO-d_6) δ 3.41 (s, 1, $\frac{1}{2}H_2O$ of hydration).

Anal. Calcd for $C_{10}H_{18}N_5O_4 \cdot \frac{1}{2}H_2O$: C, 43.47; H, 5.11; N, 25.35. Found: C, 43.51; H, 4.78; N, 25.37.

2-Amino-9-(2-deoxy-β-L-*erythro*-pentofuranosyl)purin-6-one (2′-Deoxy-L-guanosine, 15).—The entire crude sample of **14** was dissolved in 20 ml of EtOH and 40 ml of H_2O and hydrogenated at 47 psi for 15 hr in the presence of 0.09 g of 5% Pd-C. This mixture was treated as in the preparation of **12** above to yield 0.19 g (3.9% overall yield from **10**) of crystalline **15** monohydrate: $[\alpha]^{26}D$ +20.5° (*c* 1, DMF) [lit.[11] [for the D enantiomer) $[\alpha]^{26}D$ −20.3° (*c* 1.2, DMF)]; uv max (pH 1) 254 mμ (ε 12,900) and 275 sh (8900), (pH 11) 259–266 mμ (br, ε 12,000), (MeOH) 254 mμ (ε 14,700); nmr (DMSO-d_6–D_2O) δ 6.18 ("t," 1, $J_{1'-2',2''}$ = 7 Hz, H_1'), nmr (DMSO-d_6) δ 3.46 (s, 2, H_2O of hydration).

Anal. Calcd for $C_{10}H_{18}N_5O_4 \cdot H_2O$: C, 42.10; H, 5.30; N, 24.55. Found: C, 41.97; H, 5.24; N, 24.53.

The anomers **12** and **15** exhibited identical tlc mobility with their D enantiomer,[11] R_{15}/R_{12} = 1.2.

Registry No.—α anomer of **1**, 22837-36-1; β anomer of **1**, 22837-37-2; **3**, 22837-38-3; **4**, 22837-39-4; **8**, 17015-19-9; **9**, 14365-45-8; **11**, 22837-42-9; **12**, 22837-43-0; **15**, 22837-44-1.

The Hydrolysis of Cyclic Vinyl Ethers. An ^{18}O Study of the Hydrolysis of 2-Alkyl-2,3,4,5,6,7-hexahydrobenzofurans[1]

L. H. BRANNIGAN AND D. S. TARBELL

Department of Chemistry, Vanderbilt University, Nashville, Tennessee 37203

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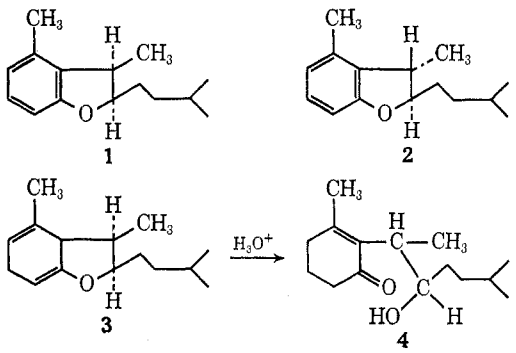
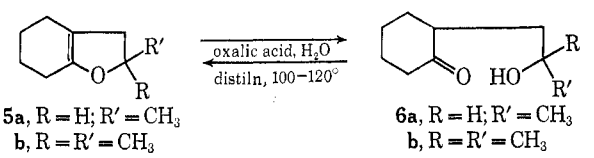
The hydrolysis of the ^{18}O-labeled cyclic vinyl ethers, 2-methyl-2,3,4,5,6,7-hexahydrobenzofuran (**5a**) and the corresponding 2,2-dimethyl compound (**5b**), followed by recyclization, leads to no loss of the ^{18}O label, within experimental error of the mass spectrometric analysis. The cracking patterns for these vinyl ethers and of 2-(2′-methoxypropyl)cyclohexanone (**8**) have been determined. The labeling experiments rule out a free carbonium ion intermediate in the hydrolysis of **5b**, where a tertiary carbonium ion could be formed; they also show that stereochemistry would be preserved around the oxygen–C-2 bond of compounds like **5a** and **5b** during acid hydrolysis.

Earlier papers[2] have reported experiments on the preparation of 2,3-dihydrobenzofurans as possible intermediates for syntheses in the fumagillin series. One of the sequences planned involved a Birch reduction[2c,3] of the 2,3-dialkyl-2,3-dihydrobenzofuran, such as **1**, followed by hydrolysis of the resulting tetrahydrobenzofuran **3**; both **1** and the corresponding *trans* compound **2** were prepared, their configurations were established, and both were reduced with lithium and liquid ammonia and then hydrolyzed.[2,3] It is obviously



necessary to know whether in the hydrolysis of the vinyl ether **3** (and the related *trans* compound) there has been cleavage of the oxygen–C-2 bond in **3**, and hence any possibility of change in the configuration of the carbon carrying the hydroxyl group in **4**.

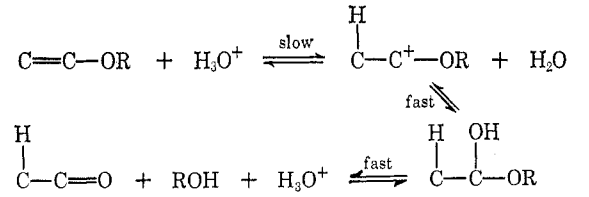
The present study shows by ^{18}O labeling studies that there is no oxygen–C-2 cleavage in compound **5a**, where C-2 carries one alkyl group, and also none in compound **5b**, where C-2 is a tertiary carbon, carrying two methyl groups.



5a, R = H; R′ = CH_3
b, R = R′ = CH_3

6a, R = H; R′ = CH_3
b, R = R′ = CH_3

Earlier studies on the mechanism of hydrolysis of acetals and of open-chain vinyl ethers have shown that, in $H_2{}^{18}O$, none of the label appears in the alcohol formed,[4] and therefore the hydrolysis does not involve cleavage of the O–R bond. Kinetic studies[5,6] and solvent isotope[6] effects indicate that the slow step is the transfer of a proton to the unsaturated carbon β to the oxygen atom, to form the resonance-stabilized carbo-



(1) Aided by Grant AI-08424 from the National Institutes of Health.

(2) (a) E. C. Hayward, D. S. Tarbell, and L. D. Colebrook, *J. Org. Chem.*, **33**, 399 (1968); (b) D. P. Brust, D. S. Tarbell, S. M. Hecht, E. C. Hayward, and L. D. Colebrook, *ibid.*, **31**, 2192 (1966); (c) D. P. Brust and D. S. Tarbell, *ibid.*, **31**, 125 (1966); (d) W. E. Harvey and D. S. Tarbell, *ibid.*, **32**, 1679 (1967).

(3) E. C. Hayward, Ph.D. Thesis, University of Rochester, 1967.

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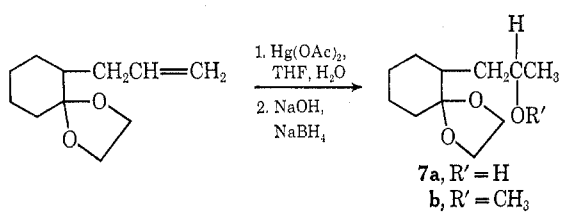
(5) D. M. Jones and N. F. Woods, *J. Chem. Soc.*, 5400 (1964); T. H. Fife, *J. Amer. Chem. Soc.*, **87**, 1084 (1965).

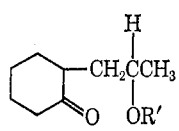
(6) A. J. Kresge and Y. Chiang, *J. Chem. Soc., B*, **53**, 58 (1967); A. J. Kresge, D. S. Sagatys, and H. L. Chen, *J. Amer. Chem. Soc.*, **90**, 4174 (1968).

nium ion,[7,8] which then forms the hemiacetal (or hemiketal); this then goes to products. There seems to be no work done on cyclic vinyl ethers of the type[2] **5**.

The labeled compounds in the 2-methyl series (**5a** and **6a**) were prepared from the known 2′-alkylcyclohexanone dioxolane[2c] by the action of mercuric acetate in THF and water containing excess ^{18}O, followed by treatment with alkali and sodium borohydride[9,10] to give the hydroxypropyl compound **7a**; this on hydrolysis with 80% acetic acid at room temperature yielded the known ketone,[2c] with the label in the hydroxyl group. The convenient method of determining the amount of ^{18}O in the hydroxyl, by forming the chlorocarbonate, decomposing the latter with organic base to form carbon dioxide, and analysis of the latter by mass spectrometry[11] was not considered applicable in the present case because of the possible interference from the carbonyl group. It is recognized that, with **7a**, **6a**,



7a, R′ = H
b, R′ = CH_3



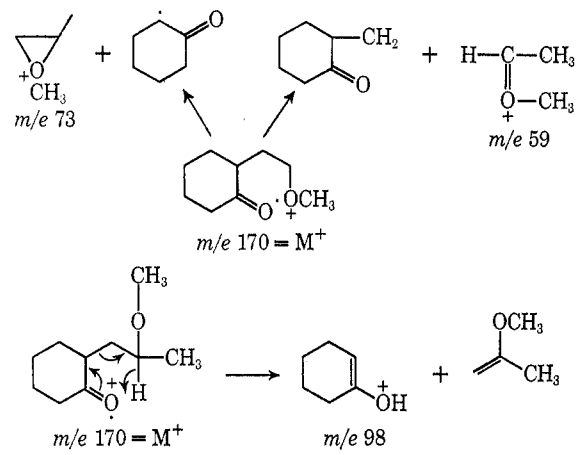
8, R′ = CH_3

and related compounds, a mixture of diastereoisomers is present, because of the asymmetric carbon in the side chain. These were usually resolved by vpc, their mass spectra were nearly identical, and hence the materials were treated as pure compounds. With the dimethyl compounds **5b** and **6b** this complication is absent.

The amount of ^{18}O incorporation in the hydroxy ketal **7a** was determined by methylation to form the methyl ether **7b**, followed by removal of the ketal group by hydrolysis in aqueous acetic acid, to the methoxy ketone **8**. The mass spectrum of labeled and unlabeled material showed clearly that the hydroxyl (and methoxyl) group was labeled to about 1%. Any ^{18}O which might have been in the carbonyl group (although there are no obvious mechanisms for its presence there) would have been exchanged off during the treatment with aqueous acetic acid.

The methoxy ketone **8**, labeled with ^{18}O in the carbonyl group, was prepared from unlabeled methoxy ketone, by the action of aqueous acetic acid containing an excess of ^{18}O.

The mass spectra of the two diastereoisomers (unlabeled) **8** are nearly identical. Both show peaks at *m/e* 59, 73, and 98, regions which are sufficiently uncomplicated to allow measurements of P + 1 and P + 2 peaks. The fragments[12] giving rise to peaks at 59 and 73 were shown to contain the ether oxygen, and the peak at 98 the carbonyl oxygen. This conclusion



was based on a comparison of the mass spectra of unlabeled **8** with that of **8** labeled at the ether oxygen and that of **8** labeled at the carbonyl oxygen. These observations are summarized in Table I. Comparison

TABLE I

COMPARISON OF THE MASS SPECTRA OF LABELED AND UNLABELED 2-(2′-METHOXYPROPYL)CYCLOHEXANONE (**8**)[a]

	Theoretical intensities		
	$C_3H_7O^+$, *m/e* 59	$C_4H_9O^+$, *m/e* 73	$C_6H_{10}O^+$, *m/e* 98
P + 1	3.39	4.51	6.68
P + 2	0.24	0.28	0.39
First Stereoisomer of **8**, Unlabeled			
P + 1	3.64	4.75	7.12
P + 2	0.31	0.38	0.54
First Stereoisomer of **8**, Ether Oxygen Labeled			
P + 1	3.61	5.18	7.52
P + 2	1.34	1.44	0.67
^{18}O incorporated	1.03	1.06	
First Stereoisomer of **8**, Carbonyl Oxygen Labeled			
P + 1	3.58	4.76	7.60
P + 2	0.32	0.39	1.50
^{18}O incorporated			0.96
Second Stereoisomer of **8**, Unlabeled			
P + 1	3.58	4.87	7.30
P + 2	0.34	0.38	0.62
Second Stereoisomer of **8**, Ether Oxygen Labeled			
P + 1	3.66	4.87	7.48
P + 2	1.15	1.21	0.73
^{18}O incorporated	0.81	0.83	
Second Stereoisomer of **8**, Carbonyl Oxygen Labeled			
P + 1	3.56	4.82	7.70
P + 2	0.32	0.39	1.60
^{18}O incorporated			0.87

[a] All figures are reported in percentage of the corresponding parent peaks.

of the P + 2 peaks associated with the peaks at 59 and 73 in the spectrum of the methoxy labeled and un-

(7) This mechanism is in agreement with the very large rate of hydrolysis of $CH_2{=}CHOC_2H_5$, compared with $(C_2H_5)_2O$, the former hydrolyzing more rapidly by a factor of 10^{13}: A. Skrabal and R. Skrabal, *Z. Phys. Chem.* (Leipzig), **181**, 459 (1938).

(8) The mechanism of hydrolysis of vinyl ethers derived from 1,3-diketones is somewhat different: L. R. Fedor and J. McLaughlin, *J. Amer. Chem. Soc.*, **91**, 3594 (1969).

(9) F. G. Bordwell and M. L. Douglass, *ibid.*, **88**, 993 (1966); H. C. Brown and P. Geoghegan, Jr., *ibid.*, **89**, 1522 (1967).

(10) R. J. Gargiulo, Ph.D. Thesis, Vanderbilt University, 1969; R. J. Gargiulo and D. S. Tarbell, *Proc. Nat. Acad. Sci. U. S.*, **62**, 52 (1969).

(11) C. J. Michejda, D. S. Tarbell and W. H. Saunders, *J. Amer. Chem. Soc.*, **84**, 4113 (1962).

(12) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962; H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964; R. M. Silverstein and G. C. Bassler, "Spectrometric Identification of Organic Compounds," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1967.

labeled ether **8** shows enrichment of ^{18}O *via* oxymercuration–demercuration of approximately 0.9%. Similarly the enrichment of ^{18}O in the carbonyl labeled compound, (**8**), by acid-catalyzed equilibration, is approximately 0.9%.

The results in Table I show the reality of ^{18}O incorporation in **7** and **8**. The question of the mechanism of the hydrolysis of the derived 2-methylhexahydrobenzofuran **5a** was answered by cyclization of the hydroxyl labeled compound **6a**; the cyclized product retained the label. Ring opening of the cyclic enol ether **5a** by 3% oxalic acid in ordinary water and THF to **6a**, followed by recyclization, gave the hexahydrobenzofuran **5a** which still contained the ^{18}O label. This is demonstrated by the data in Table II.

TABLE II

COMPARISON OF MASS SPECTRA OF LABELED AND UNLABELED 2-METHYL-2,3,4,5,6,7-HEXAHYDROBENZOFURAN (**5a**) BEFORE AND AFTER HYDROLYSIS[a]

	Theoretical intensities: $C_7H_{10}O^+$, *m/e* 110	$C_8H_{11}O^+$, *m/e* 123	$C_9H_{14}O^+$, *m/e* 138
P + 1	7.76	8.86	9.99
P + 2	0.46	0.55	0.65
Unlabeled Vinyl Ether **5a**			
P + 1	8.2	9.0	9.9
P + 2	0.5	0.7	0.7
Labeled **5a** before Hydrolysis			
P + 1	8.7	9.1	11.1
P + 2	1.7	1.8	1.8
^{18}O incorporation	1.2	1.1	1.1
Labeled **5a** after Hydrolysis and Recyclization			
P + 1	8.5	9.6	10.5
P + 2	1.6	1.8	1.8
Label lost in hydrolysis	0.1	0.0	0.0

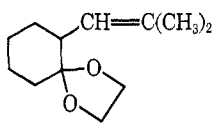
[a] All figures are reported in percentages of the corresponding parent peaks.

The mass spectrum of the cyclic vinyl ether **5a** has appropriately uncomplicated peaks at *m/e* 138 (molecular ion), 123, and 110. Comparison of the P + 2 peaks associated with the peaks at 138, 123, and 110 of labeled and unlabeled vinyl ether **5a** shows ^{18}O enrichment of 1.1%. Table II summarizes the comparison of labeled and unlabeled **5a** before and after hydrolysis, followed by recyclization.

The experimental error, estimated by the reproducibility of the P + 2 peaks relative to the respective parent peaks averaged over at least four mass spectrometer runs, was about 10%; within this error, hydrolysis of the cyclic vinyl ether **5a** to the alcohol **6a** occurs with no loss of label, and hence no disturbance of the carbon–oxygen bond in the side chain of **6a**.

The examination of the corresponding tertiary compounds **5b** and **6b** was undertaken to see if the hydrolysis of the hexahydrobenzofuran **5b** might go through a tertiary carbonium ion, which would lose the label.

2-(2′-Methylallyl)cyclohexanone[10] was converted into the ketal with ethylene glycol and *p*-toluenesulfonic acid; this resulted, as shown by the ir and nmr spectra, in an isomerization of the double bond to yield **9**; this was oxymercurated and demercurated as above in ^{18}O enriched water; and the ketal group was removed in aqueous acetic acid, forming the tertiary hydroxy



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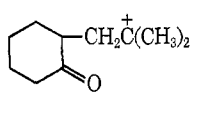


10

compound **6b**. Distillation of this yielded the 2,2-dimethylhexahydrobenzofuran **5b**, which still contained the label. Aqueous hydrolysis of **5b** to **6b**, followed by recyclization to the cyclic vinyl ether, gave a product which still contained all of the ^{18}O label, within the limits of accuracy described above. The mass spectrometric data is given in Table III. One must

TABLE III

COMPARISON OF MASS SPECTRA OF LABELED AND UNLABELED 2,2-DIMETHYL-2,3,4,5,6,7-HEXAHYDROBENZOFURAN (**5b**) BEFORE AND AFTER HYDROLYSIS[a]

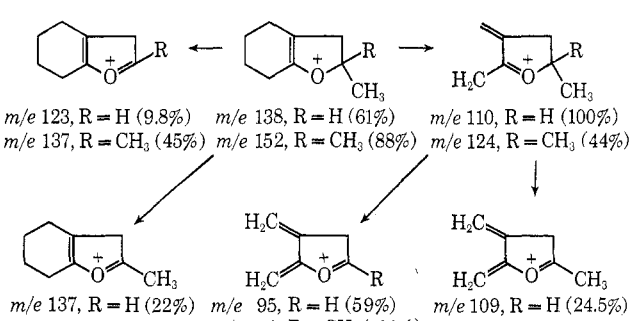
	Theoretical intensities: $C_7H_9O^+$, *m/e* 109	$C_8H_{12}O^+$, *m/e* 124	$C_{10}H_{16}O^+$, *m/e* 152
P + 1	7.75	8.88	11.10
P + 2	0.46	0.55	0.76
Unlabeled Vinyl Ether **5b**			
P + 1	15.0	8.6	12.3
P + 2	5.6	0.6	0.7
Labeled **5b** before Hydrolysis			
P + 1	14.8	9.1	12.7
P + 2	6.9	2.0	2.2
^{18}O incorporation	1.3	1.4	1.5
Labeled **5b** after Hydrolysis and Recyclization			
P + 1	15.0	9.2	12.0
P + 2	6.7	1.9	2.2
Label lost in hydrolysis	0.2	0.1	0.0

[a] All figures are reported in percentages of the corresponding parent peaks.

conclude from these results that the tertiary carbonium ion **10** is not found as a kinetically free intermediate either during the cyclization of **6b** to **5b**, or during the hydrolysis of **5b** to **6b**.

The high values for the observed P + 1 and P + 2 peaks related to the 109 peaks suggest that this is a composite peak resulting from two or more ions, and hence the values for ^{18}O incorporation derived from this figure should be disregarded.

The mass spectra fragments observed above are considered to arise by the following mechanisms.



m/e 123, R = H (9.8%) *m/e* 138, R = H (61%) *m/e* 110, R = H (100%)
m/e 137, R = CH_3 (45%) *m/e* 152, R = CH_3 (88%) *m/e* 124, R = CH_3 (44%)

m/e 137, R = H (22%) *m/e* 95, R = H (59%) *m/e* 109, R = H (24.5%)
m/e 109, R = CH_3 (100%)

Within the above experimental error, it is concluded that the acid-catalyzed hydrolysis of the Birch reduction products of 2,3-dihydrobenzofurans will give alcohols, with the stereochemistry around the oxygen–

C-2 bond identical with that of the starting 2,3-dihydrobenzofuran.

Experimental Section[13]

2-(2′-Hydroxypropyl)cyclohexanone Ketal (7a).—The ketal of 2-allylcyclohexanone[2c] (9.1 g) in 25 ml of THF was added to a mixture of 17.6 g of mercuric acetate suspended in 25 ml of THF and 2 ml of water; the latter contained approximately 1.54% excess ^{18}O and was normalized in deuterium content. After a few minutes of stirring, the mercuric acetate dissolved, giving a bright yellow solution; after 30 min, the yellow color disappeared. The slightly cloudy solution was stirred an additional 30 min. The mixture was cooled in an ice bath and the rapid addition of 50 ml of 3 *M* NaOH was followed by dropwise addition of 50 ml of 0.05 *M* $NaBH_4$ in 3 *M* NaOH. The precipitated mercury was allowed to settle overnight. The aqueous layer was then saturated with sodium chloride and the tetrahydrofuran layer was separated. The water layer was extracted with two 50-ml portions of ethyl ether. The combined tetrahydrofuran and ether solutions were dried, filtered, and the solvents were removed on the rotary evaporator. The liquid residue was distilled through an 8-in. vacuum-jacketed Vigreux column. Two fractions were collected: 0.9 g, bp 52–57° (0.2 mm); and 6.5 g, bp 86–88° (0.15 mm). The nmr and ir spectra of the high boiling fraction were identical with those reported[2c] for the ketal **7a**.

The following preparations were carried out on both labeled and unlabeled materials, following identical procedures.

2-(2′-Hydroxypropyl)cyclohexanone (6a).—The above ketal (4.5 g) was stirred in 10 ml of 80% acetic acid at room temperature for 50 hr. The solution was diluted with 50 ml of water and worked up in conventional fashion. Distillation yielded two fractions: 0.4 g, bp 45° (0.1 mm); and 3.0 g (84%) bp 55–57° (0.04–0.05 mm). The high boiling fraction had nmr and ir spectra identical with those reported for 2-(2′-hydroxypropyl)-cyclohexanone.[2c,d]

2-(2′-Methoxypropyl)cyclohexanone (8).—The ketal **7a** (750 mg) was methylated with sodium hydride–methyl iodide in a mixture of ether and DMF. The product was hydrolyzed in 80% acetic acid by standing overnight at room temperature. A standard workup gave about 500 mg of a light yellow liquid. Vapor phase chromatography on a 10 ft × 1/4 in. Ucon Polar column (column temperature, 145°; flow rate, 60 ml of He/min) showed five peaks. The peaks had retention times of 2.2, 3.6, 4.8, 10.2, and 12.8 min. The latter two peaks, not fully resolved, were about 50% of the mixture, and were shown by co-injection to be identical with the diastereomeric mixture of 2-(2′-methoxypropyl)cyclohexanone (**8**) prepared by a different method.[10] The two peaks at 10.2 and 12.8 min were collected together, and the colorless liquid obtained was evaporatively distilled (bath temperature 80°, 1 mm).

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.23; H, 10.61.

Two completely resolved peaks were observed when the above analytical sample was injected onto a 10 ft × 1/8 in. 10% SE-30 column (column temperature, 120°) eluting at 6.7 and 8.9 min. Mass spectra of the two components were run on the eluent from a 9 ft × 1/8 in. 3% OV-1 column. The mass spectra of the two components were nearly identical, indicating that they are diastereoisomers. The mass spectra of the unlabeled diastereoisomers were obtained from a 6 ft × 0.25 in. 1% SE-30 column.

The unlabeled 2-(2′-methoxypropyl)cyclohexanone (**8**) was labeled at the carbonyl oxygen by standing for 2 hr at room temperature in 80% acetic acid, containing ^{18}O enriched water, as above. The product was shown by vpc to be almost pure **8**; the mass spectra of the two diastereoisomers were obtained from the eluent from a 6 ft × 0.25 in. 1% SE-30 column.

2-Methyl-2,3,4,5,6,7-hexahydrobenzofuran (5a).—2-(2′-Hydroxypropyl)cyclohexanone (labeled with ^{18}O as above, **4g**) was distilled through a 4-in. Vigreux column at 20 mm (bath temperature, 100°). After a small amount of water had been distilled, 3.2 g (78%) of 2-methyl-2,3,4,5,6,7-hexahydrobenzofuran, bp 68° (20 mm) [lit.[2d] bp 85–86° (30 mm)], was collected. The nmr and ir spectra were identical with those previously reported.[2d] The mass spectrum of this compound was obtained from the single peak eluting from the 6 ft × 0.25 in. 1% SE-30 column of the mass spectrometer.

Hydrolysis of 2-Methyl-2,3,4,5,6,7-hexahydrobenzofuran (5a).—A solution of 3.0 g of the hexahydrobenzofuran **5a** was allowed to stand at room temperature for 10 hr in a mixture of 5 ml of THF and 5 ml of distilled water containing 300 mg of oxalic acid. The solution was diluted with 25 ml of distilled water. The aqueous layer was separated and extracted with five 25-ml portions of ethyl ether, and the combined tetrahydrofuran and ether solutions were washed with water, 10% sodium bicarbonate, and again with water. The ether–tetrahydrofuran solution was dried and filtered; the solvents were removed by evaporating under reduced pressure. The liquid residue (2.4 g) was distilled through a 4-in. Vigreux column, giving two fractions: 0.2 g, bp approximately 45° (0.1 mm); and 1.9 g (56%), bp 57° (0.06 mm). The fraction boiling at the higher temperature had nmr and ir spectra identical with those of the 2-(2′-hydroxypropyl)cyclohexanone (**6a**) previously prepared.

Recyclization of the 2-(2′-Hydroxypropyl)cyclohexanone (6a) from Hydrolysis of 2-Methyl-2,3,4,5,6,7-hexahydrobenzofuran (5a).—Distillation of about 1 g of the 2-(2′-hydroxypropyl)-cyclohexanone, obtained from hydrolysis of 2-methyl-2,3,4,5,6,7-hexahydrobenzofuran, through a 4-in. Vigreux column provided about 500 mg of regenerated **5a**. The mass spectrum of this sample was obtained from the single peak eluting from a 6 ft × 1/4 in. 1% SE-30 column.

2-(2′-Methylallyl)cyclohexanone was prepared by oxidation of *trans*-2-(2′-methylallyl)cyclohexanol[14] with chromic oxide, sulfuric acid, acetone, and water. The product was obtained in 65% yield and had appropriate ir and nmr spectra, as well as other properties previously reported.[10,15] The ethylene ketal of 2-(2′-methyl-1′-propenyl)cyclohexanone (**9**) was prepared from the 2-(2′-methylallyl)cyclohexanone by the usual procedure with ethylene glycol, benzene, and *p*-toluenesulfonic acid. Distillation of the product gave a 53% yield of **9**, bp 59–62° (0.07 mm). Vapor phase chromatography on a 3% SE-30 column (column temperature, 130°; flow rate, 60 ml of He/min) showed peaks at 5.3, 7.3, and 8 min. The peak at 7.3 min was about 90% of the mixture. Vapor phase chromatography on a 5 ft × 0.25 in. 25% QF-1 column (column temperature, 155°; flow rate, 60 ml of He/min) showed peaks at 8.7 and 10.6 min. The major peak at 8.7 min was collected and evaporatively distilled (bath temperature, 80°, pressure, 1 mm). Reinjection of this sample showed that it was at least 98% pure. The ir and nmr spectra were in complete agreement with structure **9**.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.33; H, 10.24.

Hydroxylation of the unsaturated ketal 9 was carried out in ^{18}O enriched water *via* mercuration, as described above. The product was separated into two fractions by distillation: 3.8 g, bp 43–49° (0.15 mm); and 4.2 g (39% yield) bp 81–82° (0.15 mm). The first fraction was identified as starting material by vpc. Vpc of the high boiling fraction on a 5 ft × 0.25 in. 3% SE-30 column (column temperature, 145°; flow rate, 60 ml of He/min) showed one major peak at 5.3 min. This peak was collected and evaporatively distilled (bath temperature, 80°; pressure, 1 mm). The ir and nmr spectra were in agreement with the structure of the expected hydroxy ketal.

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.25; H, 10.35. Found: C, 67.47; H, 10.36.

2-(2′-Methyl-2′-hydroxypropyl)cyclohexanone (6b).—The ketal of this compound, prepared above, was hydrolyzed in 80% acetic acid at room temperature for 14 hr (3.8 g in 20 ml). The reaction mixture yielded, after a standard work-up, 3.0 g of a viscous oil, which had ir and nmr spectra consistent with those expected for the desired compound **6b**. Vapor phase chromatography of this oil on a 5 ft × 0.25 in. 25% QF-1 column (column temperature, 125°; flow rate, 60 ml of He/min) showed sharp peaks at 5.3 and 8.5 min in a ratio of about 20:1, respectively.

(13) Microanalyses were done by Galbraith Laboratories, Inc., Knoxville, Tenn. All melting points and boiling points are uncorrected. The infrared spectra were taken on a Beckman IR-10 spectrophotometer in solutions or liquid films, as indicated for each compound. The nmr spectra were recorded on a Varian A-60 spectrometer in carbon tetrachloride; all chemical shifts are reported in parts per million (δ) with TMS as internal standard. Vapor phase chromatography was done on the Varian-Aerograph Model 90-P or A90-P, or the F & M Model 720 or 700. Mass spectra were obtained from an LKB Type 9000 mass spectrometer; we are greatly indebted to Mr. C. T. Wetter and Mrs. Betty Fox for the mass spectrometric data.

(14) Prepared by Dr. R. J. Gargiulo,[16] from β-methylallylmagnesium chloride and cyclohexene oxide, following the procedure of H. Felkin and G. Roussi, *Tetrahedron Lett.*, 4153 (1965).

(15) S. E. Cantor and D. S. Tarbell, *J. Amer. Chem. Soc.*, **86**, 2902 (1964).

The peak at 8.5 min was identified as the starting material by coinjection. The larger peak was collected and identified as the cyclic vinyl ether **6b** by coinjection with a sample prepared according to the procedure described in the next section.

The crude material (about 3 g) from a run similar to the above was distilled under vacuum. A small amount of a substance, bp, 43–46° (0.025 mm), was collected. The ir spectrum had weak bands in the hydroxyl and carbonyl regions and the nmr spectrum showed that the dioxolane ring was present. This oil was apparently a mixture of the starting material and the desired ketoalcohol **6b**. As this low boiling fraction was distilled, white needles began to form in the column. The distillation was stopped and the residue in the distilling flask was taken up in 4 ml of petroleum ether. The solution was chilled in the freezer and seeded with the crystals which had formed in the column. After 24 hr, a crop of white needles (1.4 g) had separated. Two subsequent recrystallizations from petroleum ether gave 1.2 g, mp 59–60°, of analytically pure 2-(2′-methyl-2′-hydroxypropyl)-cyclohexanone (**6b**). Concentration of the mother liquors gave another 0.9 g, mp 57–60°; total yield was 68%. When a solution of the oil, in petroleum ether, which had not been subjected to distillation, was cooled in the freezer, white needles were obtained, mp 57–59°. The mmp 57–59.5° of the sample obtained from the distillation and that obtained from direct crystallization from petroleum ether showed no depression. The ir spectrum ($CHCl_3$) showed absorption at 3400 cm^{-1} (hydroxyl), 1710 (ketone), 1360 and 1375 (*gem*-dimethyl group), 1150, 1050, and 930 cm^{-1}. The ketone absorption was of moderate strength, while the hydroxyl band was strong. The nmr spectrum (CCl_4) had a doublet at 1.32 ppm (6 H, methyl protons), a complex envelope from 1.4 to 2.2 (10 H, ring and chain protons), a complex multiplet at 2.25 (1 H, tertiary proton α to carbonyl), and a broad absorption at 3.3 (1 H, hydroxyl proton).

When the crystalline solid was vaporized into the ionizing chamber of the mass spectrometer two substances were observed. The substance which vaporized first showed a molecular ion at *m/e* 170, which was verified by running the scan at 12 eV instead of the normal 70 eV. This is a molecular weight consistent with that expected for the desired ketoalcohol. The second substance which was vaporized showed a molecular ion of *m/e* 322. This second compound was not identified conclusively, but it was apparently a dimer of the keto alcohol **6b**, which is in equilibrium with the keto alcohol **6b** itself. The analysis reported below was performed on the crystalline solid above.

Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.54; H, 10.66. Found: C, 70.30; H, 10.66.

2,2-Dimethyl-2,3,4,5,6,7-hexahydrobenzofuran (5b).—The crude oily product from the preceding experiment was distilled under reduced pressure (water pump). From the 3.0 g of **6b** which was distilled (bath temperature, 120°; pressure, 15 mm), 2.1 g (75%) of a colorless liquid was collected, bp 85° (15 mm). Vapor phase chromatography of this product on a 5 ft × 0.25 in. 25% QF-1 column (column temperature, 125°; flow rate, 60 ml of He/min) showed one peak at 5.3 min. This peak was collected and evaporatively distilled (bath temperature, 70°; pressure, 15 mm). The ir spectrum (liquid film) showed bands at 1710 cm^{-1} (enol ether), 1445, 1370, and 1385 (*gem*-dimethyl group), 1300, 1270, and 1220 (ether C–O), and 1195, 1150, 1095, 905, 870, and 785. There was also a weak band in the hydroxyl region of the spectrum, indicating that some alcohol was still present. The nmr spectrum (CCl_4) showed a singlet at 1.26 ppm (6 H, methyl groups), a multiplet at 1.65 (4 H, protons of the six-membered ring), a multiplet at 1.92 (4 H, allylic protons of the six-membered ring), and a multiplet at 2.25 (2 H, allylic protons of the five-membered ring). The mass spectrum of this compound was obtained from the single peak eluting from a 6 ft × 0.25 in. 1% SE-30 column. A satisfactory analysis was not obtained, probably owing to the presence of the keto alcohol, and the ease of hydrolysis of the enol ether.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 77.03; H, 10.41.

Hydrolysis and recyclization of **5b** and **6b** were carried out as previously described for the monomethyl compounds **5a** and **6a**. The physical properties of the compounds obtained in this way were identical with the physical properties of the samples obtained earlier.

Registry No.—**5a**, 10198-31-9; **5b**, 22931-91-5; **6b**, 22931-92-6; **8**, 22931-93-7; **9**, 22931-94-8; ethylene ketal of **6b**, 22931-95-9.

Hydrogenation of Cycloalkenes Using Homogeneous Rhodium Complexes as Catalysts[1]

ALLEN S. HUSSEY AND YOSHINOBU TAKEUCHI

Ipatieff Catalytic Laboratory, Department of Chemistry, Northwestern University, Evanston, Illinois 60201

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Initial rates of hydrogenation and pseudo-first-order rate constants are reported for several cycloalkenes in different solvent systems at 25.0 ± 0.1° under 1 atm of hydrogen using rhodium complexes as homogeneous catalysts. None of the solvent systems investigated has been found to be more effective than 3:1 benzene–ethanol. 1,2-Dimethylcyclohexene (**1**) and 1,3-dimethylcyclohexene (**3**) are not hydrogenated with chlorotris(triphenylphosphine)rhodium(I), nor is 1-methylcyclohexene (**2**) with either a diphenylpiperidylphosphine or a phenyldipiperidylphosphine complex. Deuterium addition to bicyclo[2.2.1]heptene (**8**) is *exo,cis*. 2,3-Dimethylcyclohexene (**5**) and 2,4-dimethylcyclohexene (**6**) furnish 50% and 48% *cis* products, respectively, and their thermodynamically less stable product isomers are appreciably more exchanged than are their more stable counterparts when deuterium is used. These results permit refinements of the mechanistic details of this reaction.

Alkylcyclohexenes with trisubstituted double bonds are hydrogenated rather slowly relative to cyclohexene using Wilkinson's chlorotris(triphenylphosphine)rhodium(I) catalyst[2] in benzene–ethanol at 25° under 1 atm of hydrogen pressure.[3] We report here the use of this catalyst, as well as variants of it,[4,5] in the hydrogenation of 1,2-dimethylcyclohexene (**1**), 1-methylcyclohexene (**2**), 1,3-dimethylcylohexene (**3**), 1,4-dimethylcyclohexene (**4**), 2,3-dimethylcyclohexene (**5**), 2,4-dimethylcyclohexene (**6**), *p*-menthene (**7**), and bicyclo[2.2.1]hept-2-ene (**8**) in benzene and benzene–ethanol solution. The effect of several other solvent systems on the rates of hydrogenation of **2** has also been investigated.

Experimental Section

Apparatus and Procedures.—With chlorotris(triphenylphosphine)rhodium(I) as the catalyst, the procedures were described

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