Conclusion

The oxymercuration–demercuration of olefins has previously been shown to be a highly convenient synthetic method for the Markovnikov hydration of olefins. The present paper has demonstrated a wide range of reactivity accompanying variation of olefin structure. Accordingly, considerable selectivity in the monooxymercuration of dienes is expected. Steric factors play a major role in determining the reactivity of hydrocarbon olefins. Thus, increased substitution on the double bond (as long as the carbonium ion stability remains the same) and increased steric hindrance at the site of hydroxyl or mercury substituent attachment decrease the rate of reaction. Increased stability of the carbonium ion or decreased stability of the olefinic ground state due either to increased cis interactions or constraint in a bicyclic ring system increase the reactivity of the double bond. However, since the situation appears to be relatively complex, it appears best to proceed from experimental data on the relative reactivities of known structures to predict the results of competitive oxymercuration of mixtures of olefins. As will be pointed out in the following paper,[7] the data are helpful in predicting the course of monohydration of dienes.

Experimental Section

Materials.—All olefins used were commercially available and were used as obtained unless vpc or index of refraction data indicated impurities. Mercuric acetate (Mallinckrodt Chemical Works), sodium borohydride (Metal Hydrides, Inc.), and tetrahydrofuran (Fisher Scientific Co.) were used without further purification.

Oxymercuration Procedure.—The general procedure used has been discussed in the text. Cyclohexene was used as the reference olefin in all cases except the following. Norbornene was determined relative to styrene and also relative to 1-pentene. α-Methylstyrene was determined relative to styrene. 2,4,4-Trimethyl-2-pentene, bicyclo[2.2.2]oct-2-ene, and cyclooctene were all determined relative to 2,3-dimethyl-2-butene. In all cases where a reference olefin other than cyclohexene was used, the k_r value was back-calculated to cyclohexene for purposes of presentation in the text.

Control Experiment.—In order to establish that the mercurials do not equilibrate under the reaction conditions employed, the following experiment was performed. Cyclohexene and 1-hexene were oxymercurated separately for 15 min on a 10-mm scale employing 10 mm of mercuric acetate, 10 ml of water, and 10 ml of THF for each olefin; 30 ml of THF was then added to each reaction mixture and the solutions were cooled to 0°. To each reaction mixture was added 10 mm of the other olefin and the solutions were stirred for 8 hr at 0°. Reduction of the mercurials and subsequent vpc analysis showed that no more than 3% of the mercurial from either olefin was converted into the mercurial of the other olefin.

Registry No.—3-Methyl-1-butene, 563-45-1; 1-hexene, 592-41-6; 3,3-dimethyl-1-butene, 558-37-2; 1-pentene, 109-67-1; 2,4-dimethyl-2-pentene, 625-65-0; cyclopentene, 142-29-0; *cis*-4-methyl-2-pentene, 691-38-3; *cis*-2-pentene, 627-20-3; *trans*-2-pentene, 646-04-8; *trans*-4-methyl-2-pentene, 674-76-0; 2-methyl-1-pentene, 763-29-1; 2-methyl-2-pentene, 625-27-4; 2,4,4-trimethyl-2-pentene, 107-40-4; 2,3-dimethyl-2-butene, 563-79-1; cyclohexene, 110-83-8; 1-methylcyclopentene, 693-89-0; methylenecyclopentane, 1528-30-9; cyclooctene, 931-88-4; norbornene, 498-66-8; bicyclo[2.2.2]octene, 931-64-6; styrene, 100-42-5; α-methylstyrene, 98-83-9; *cis*-propenylbenzene, 766-90-5; *trans*-propenylbenzene, 873-66-5; 2-methyl-1-propene, 115-11-7; 1-butene, 106-98-9; *cis*-2-butene, 590-18-1; *trans*-2-butene, 624-64-6.

Solvomercuration–Demercuration. IV. The Monohydration of Representative Dienes *via* Oxymercuration–Demercuration

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The oxymercuration–demercuration of dienes with 1 mol of mercuric acetate per mole of diene under standard conditions (80% aqueous tetrahydrofuran) provides a convenient procedure for the Markovnikov monohydration of one of the two double bonds in the diene. In the case of symmetrical nonconjugated dienes, such as 1,5-pentadiene, 1,7-octadiene, and 1,11-dodecadiene, the yield of enol is lower than predicted for a statistical reaction (50% enol) but approaches the statistical value with the longer chains. The yields can be raised by using mercuric trifluoroacetate. In the case of unsymmetrical dienes, such as 2-methyl-1,11-dodecadiene, 11-methyl-1,10-dodecadiene, 4-vinylcyclohexene, and limonene, the yields of enols are higher and involve selective hydration of the double bond whose structural features indicate it to be the more reactive on the basis of the related study of the relative reactivities of representative olefins under these conditions. Good yields of enols can also be realized from conjugated dienes provided that the reaction time is minimized.

Hydroboration–oxidation provides a convenient procedure for the anti-Markovnikov hydration of the carbon–carbon double bonds in olefins and dienes.[5,6] Oxymercuration–demercuration provides an equally convenient procedure for the Markovnikov hydration of the carbon–carbon double bonds in olefins[7] and dienes.[8]

Although there have been a number of reports of the monosolvomercuration of dienes, a systematic study of the synthetic utility of the reaction for the synthesis of enols *via* the monohydration of dienes has not been

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[3] National Science Foundation Fellow at Purdue University, 1967–1969.

[4] National Science Foundation Trainee at Purdue University, 1969–1971.

[5] H. C. Brown, "Hydroboration," W. A. Benjamin, New York, N. Y., 1962.

[6] G. Zweifel and H. C. Brown, *Org. React.*, **13**, 1 (1963).

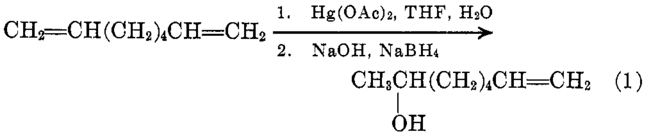
[7] H. C. Brown and P. J. Geoghegan, Jr., *J. Org. Chem.*, **35**, 1844 (1970).

[8] H. C. Brown, P. J. Geoghegan, Jr., J. T. Kurek, and G. J. Lynch, *Organometal. Chem. Syn.*, **1**, 7 (1970/1971).

available. Indeed, much of the previous research involving dienes has been concerned more with the mechanism of either the oxymercuration stage[9] or the reduction stage[10] than with the synthetic application of the reaction.

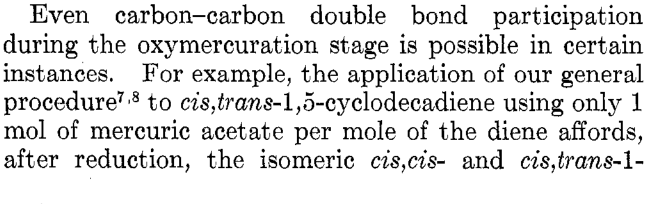
Accordingly, we decided to examine the feasibility of achieving the Markovnikov monohydration of representative dienes utilizing our general procedure.[7,8] Two minor modifications in this procedure were made. In order to minimize possible complications arising from immiscibility of the diene in the reaction mixture, we adopted a less aqueous system, 80% (v/v) tetrahydrofuran–20% water. (The standard procedure utilized a 50:50 mixture.[7,8]) We also utilized a lower temperature, 0°, in many cases in order to enhance the possibility for selective reaction and to minimize the possibilities for side reactions in certain systems. Finally, the 80:20 aqueous THF system and 0° temperature corresponded to the conditions we had utilized in our study of the relative reactivity of various olefin structures.[11]

It should be pointed out that the available data make it clear that several complicating factors may intervene to interfere with the proposed synthesis. If the oxymercuration of a symmetrical diene, such as 1,7-octadiene, were purely statistical, the maximum conversion to the desired 7-octen-2-ol (eq 1) would be 50% (25% diene, 50% enol, 25% diol). However, if the monooxymercurated product were more reactive or its further reaction were favored by physical factors, the yield of enol could be greatly diminished.



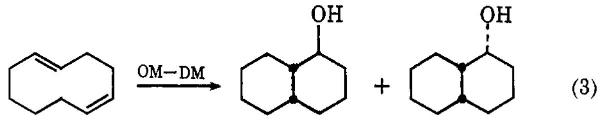
$$CH_2{=}CH(CH_2)_4CH{=}CH_2 \xrightarrow[\text{2. NaOH, NaBH}_4]{\text{1. Hg(OAc)}_2\text{, THF, H}_2\text{O}} \underset{\displaystyle OH}{CH_3\underset{|}{C}H}(CH_2)_4CH{=}CH_2 \quad (1)$$

Participation by the hydroxy group of the initial product can lead to the formation of ethers[8,10d] (eq 2).

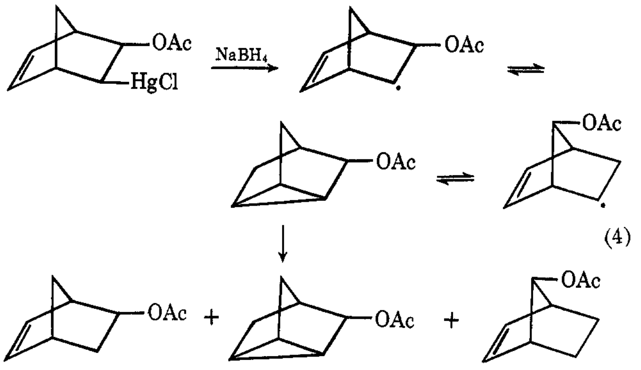


This side reaction can reduce the yield of the desired monohydration product to essentially zero.

Even carbon–carbon double bond participation during the oxymercuration stage is possible in certain instances. For example, the application of our general procedure[7,8] to *cis,trans*-1,5-cyclodecadiene using only 1 mol of mercuric acetate per mole of the diene affords, after reduction, the isomeric *cis,cis*- and *cis,trans*-1-decalols[12] (eq 3). Similarly, norbornadiene under kinetic control gives only cis-2,3-exo oxymercuration. On the other hand, under thermodynamic control, the intermediate mercurial is nortricyclenic.[13]



The reduction of the oxymercurial apparently proceeds *via* a free radical intermediate. This can react with neighboring carbon–carbon double bonds and produce new structures. For example, the cis-2,3-exo oxymercuration product from norbornadiene is converted into a mixture of at least three isomeric alcohols upon reduction with sodium borohydride[10a–c] (eq 4).



This study was undertaken in the hope of establishing the type of dienes which could be monohydrated without serious interference by these side reactions.

Results and Discussion

The general procedure which was followed was to add 10 mmol of diene to a mixture of 10 ml of water and 40 ml of tetrahydrofuran (THF). The reaction mixture was then brought to reaction temperature, usually 0°, and 10 mmol of mercuric acetate was added. The mixture was stirred for the time indicated (T_2), and 10 ml of a 3 *M* solution of sodium hydroxide was added, followed by 10 ml of a 0.5 *M* solution of sodium borohydride in 3 *M* sodium hydroxide. After 0.5 hr, a suitable glpc standard was added and the aqueous phase was saturated with potassium carbonate. The THF phase was separated, dried, and analyzed by glpc. To achieve more quantitative recovery of certain highly water-soluble products, the aqueous phase was further extracted with THF in some instances.

Symmetrical Nonconjugated Dienes.—1,4-Pentadiene, 1,7-octadiene, and 1,11-dodecadiene were selected for detailed study. [1,5-Hexadiene was not included because it was known from previous work that the oxymercuration stage would lead predominantly to the cyclic ether[8,10d] (eq 2).] The results are summarized in Table I.

It is evident that the yield of enol is considerably lower than the value predicted on the basis of a statistical attack of the mercurating agent on the double bond. As the chain length increases, the yield rises, approaching the 50% yield predicted on the basis of a

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[9] The following reviews provide a guide to the voluminous literature: (a) J. Chatt, *Chem. Rev.*, **48**, 7 (1951); (b) N. S. Zefirov, *Usp. Khim.*, **34**, 1272 (1965); *Russ. Chem. Rev.*, **34**, 527 (1965); W. Kitching, *Organometal. Chem. Rev.*, **3**, 61 (1968).

[10] The following papers involve pertinent studies of the mechanism of the reduction stage: (a) G. M. Whitesides and J. S. Filippo, Jr., *J. Amer. Chem. Soc.*, **92**, 6611 (1970); (b) G. A. Grey and W. R. Jackson, *ibid.*, **91**, 6205 (1969); (c) D. J. Pasto and J. A. Gontarz, *ibid.*, **91**, 719 (1969); (d) F. G. Bordwell and M. L. Douglass, *ibid.*, **88**, 993 (1966).

[11] H. C. Brown and P. J. Geoghegan, Jr., *J. Org. Chem.*, **37**, 1937 (1972).

[12] J. G. Traynham, G. R. Franzen, G. A. Knesel, and D. J. Northington, Jr., *ibid.*, **32**, 3285 (1967).

[13] K. C. Pande and S. Winstein, *Tetrahedron Lett.*, 3393 (1964).

TABLE I
MONOOXYMERCURATION–DEMERCURATION OF SYMMETRICAL NONCONJUGATED DIENES WITH MERCURIC ACETATE IN AQUEOUS TETRAHYDROFURAN (80%)

Diene	Temp, °C	Time, t_2,[a] hr	Yield,[b] % Diene	Enol[c]	Diol[d]
1,4-Pentadiene	0	0.5		16	
	0	2.0		16	
	25	0.5	35	12	
	25	2.0	31	13	
1,7-Octadiene	0	0.5		19	28
	0	2.0		18	29
	25	0.5	45	21	37
	25	2.0	45	18	36
1,11-Dodecadiene	0	2.0	33	40	28
	25	1.0	30	41	30

[a] Reaction time for addition of mercuric acetate to addition of base. [b] By glpc analysis. [c] $CH_2{=}CH(CH_2)_nCH(OH)CH_3$. [d] $CH_3CH(OH)(CH_2)_nCH(OH)CH_3$.

statistical oxymercuration of the two identical double bonds.

It is evident from the results for 1,7-octadiene that the low yield is primarily the result of the formation of diol in amounts greater than would be anticipated on a purely statistical basis. With the two reaction centers so widely separated, it is difficult to believe that the oxymercurial moiety at one end can influence the preferred reaction of the remaining double bond at the other end of the chain. It appears more likely that this is primarily the result of physical factors, such as partial miscibility and reaction at interphases. However, this question, interesting as it is, was considered to be beyond the range of our present objectives and was not pursued.

It appeared that the use of a more soluble mercury salt might alter the results. Indeed, the use of mercuric trifluoroacetate did increase the yield of enol (Table II).

TABLE II
MONOOXYMERCURATION–DEMERCURATION OF SYMMETRICAL NONCONJUGATED DIENES WITH MERCURIC TRIFLUOROACETATE IN AQUEOUS TETRAHYDROFURAN (80%)

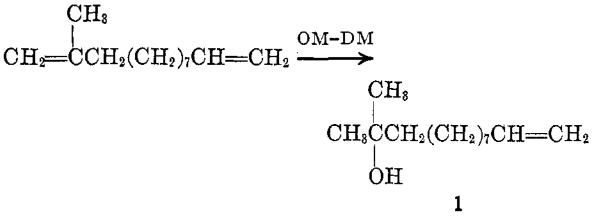
Diene	Temp, °C	Time, t_2,[a] hr	Yield,[b] % Diene	Enol[c]	Diol[d]
1,4-Pentadiene	0	0.5		26	
	0	2.0		27	
	25	2.0		47	
	25	4.0		53	
	25	8.0		57	
1,7-Octadiene	0	0.5		31	16
	0	2.0		31	20
	25	2.0	26	41	19[e]
	25	4.0	26	42	17[e]
1,11-Dodecadiene	0	2.0	37	46	18

[a–d] See corresponding footnotes in Table I. [e] Small amounts (1–4%) of *cis*- and *trans*-2,7-dimethyloxepanes were identified.

At 0° the constancy of the yields with time indicates that these are the kinetic products. However, the increase in the yields of enol with time at 25° indicates that we may be observing an equilibration. In any event, we are approaching essentially the statistically possible yield of 50% enol in all three cases.

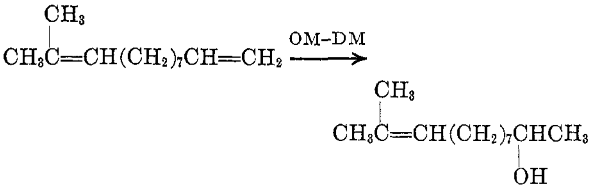
Unsymmetrical Nonconjugated Dienes.—2-Methyl-1,11- and 11-methyl-1,10-dodecadiene were selected to test the feasibility of achieving a selective monohydration of unsymmetrical acyclic dienes. Limonene and 4-vinylcyclohexene were selected as examples of unsymmetrical cyclic dienes.

It was previously reported that under these oxymercuration conditions 2-methyl-1-pentene is approximately seven times as reactive as 1-pentene.[11] Similarly, 1-pentene is five times as reactive as 2-methyl-2-pentene.[11] If these relative reactivities can be carried over to the test dienes, the monohydrations should proceed predominantly as indicated in eq 5 and 6.



$$CH_2{=}C(CH_3)CH_2(CH_2)_7CH{=}CH_2 \xrightarrow{\text{OM-DM}} CH_3C(CH_3)(OH)CH_2(CH_2)_7CH{=}CH_2 \quad (5)$$

1



$$CH_3C(CH_3){=}CH(CH_2)_7CH{=}CH_2 \xrightarrow{\text{OM-DM}} CH_3C(CH_3){=}CH(CH_2)_7CH(OH)CH_3 \quad (6)$$

2

Indeed, this is observed. The enols **1** and **2** are each obtained from their respective dienes in yields of 55%, with the isomeric enols formed in only very minor amounts, 2 and 1%.

The reactivity data for simple olefins[11] predict that the monohydration of limonene should proceed as shown in eq 7. Indeed, the reaction takes the predicted course (Table III).

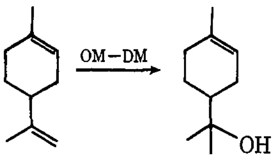


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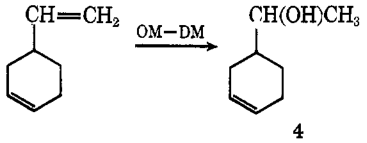
TABLE III
MONOOXYMERCURATION–DEMERCURATION OF UNSYMMETRICAL NONCONJUGATED DIENES WITH MERCURIC ACETATE IN AQUEOUS TETRAHYDROFURAN

Diene	Temp, °C	Time, t_2,[a] hr	Yield,[b] % Diene	Enol$_1$	Enol$_2$[c]	Diol
2-Methyl-1,11-dodecadiene	25	1.0	16	55[e]	1	15[i]
11-Methyl-1,10-dodecadiene	25	1.0	18	55[f]	2	14[i]
Limonene[d]	25	0.5	19	70[g]		7[j]
4-Vinylcyclohexene	25	0.5	42	12[h]	(2)[l]	22[k]
4-Vinylcyclohexene[d]	25	2.0	37	21[h]	(3)[l]	21[k]

[a,b] See corresponding footnotes in Table I. [c] Isomeric enol. [d] 50% aqueous THF. [e] **1**. [f] **2**. [g] **3**. [h] **4**. [i] 2-Methyl-2,11-dodecanediol. [j] Isomeric di-*tert*-diols. [k] Plus approximately 10% bicyclic ethers also formed. [l] Presumably isomeric enols, but not characterized.

Finally, the reactivity data indicate that both unsaturated centers in 4-vinylcyclohexene possess com-



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(8)

parable reactivity.[11] Consequently, a simple conversion to the secondary alcohol **4** would not be anticipated. Indeed, the results (Table III) reveal that **4** is formed only in modest yield. There are formed both isomeric enols and cyclic ethers. Fortunately, as discussed below, the use of mercuric trifluoroacetate overcomes this difficulty.

Consequently, it is now possible to achieve the Markovnikov monohydration of the exocyclic double bond in limonene and 4-vinylcyclohexene *via* oxymercuration–demercuration. It is of interest to point out that hydroboration of these two dienes with disiamylborane, followed by oxidation with alkaline hydrogen peroxide, yields the corresponding primary enols in these cases.[5,6]

The monohydration of some of these dienes with mercuric trifluoroacetate was also examined. The results are summarized in Table IV.

Table IV

Monooxymercuration–Demercuration of Unsymmetrical Nonconjugated Dienes with Mercuric Trifluoroacetate in Aqueous Tetrahydrofuran

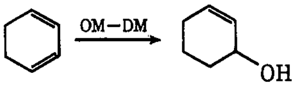
Diene	Temp, °C	Time, t_2,[a] hr	Yield,[b] %: Diene	Enol$_1$	Enol$_2$[c]	Diol
2-Methyl-1,11-dodecadiene	0	0.16	24	43[d]	4	17[g]
	25	1.0	26	18[d]	26	22[g]
11-Methyl-1,10-dodecadiene	0	0.16	24	48[e]	5	18[g]
	25	1.0	8	83[e]	1	2[g]
4-Vinylcyclohexene	0	0.1	32	16[f]	(10)[i]	24[h]
	25	0.1	25	37[f]	(4)[i]	18[h]
	25	0.5	18	60[f]	(2)[i]	7[h]
	25	2.0	14	55[f]	(2)[i]	7[h]

[a,b] See corresponding footnotes in Table I. [c] Isomeric enol. [d] **1**. [e] **2**. [f] **4**. [g] 2-Methyl-2,11-dodecanediol. [h] Bicyclic ethers plus diol. [i] Presumably isomeric enols, but not characterized.

Perhaps the most noteworthy feature is the increase in the yield of the enol **2** from 55% under kinetic conditions with mercuric acetate (Table III) to 83% under equilibrating conditions with mercuric trifluoroacetate. Similarly the yield of 62% of enol **4** under these conditions is far higher than that achieved under the kinetic conditions of the reaction involving mercuric acetate. It has been noted in other studies in this laboratory that deoxymercuration of the mercuric trifluoroacetate adduct is considerably more rapid for olefins containing internal di- and trisubstituted double bonds than for terminal olefins. Consequently, the use of mercuric trifluoroacetate at 25° with longer reaction times may provide the basis for a general method to shift the oxymercurial adduct from an internal position to a terminal position.

Conjugated Dienes.—2,3-Dimethyl-1,3-butadiene and 1,3-cyclohexadiene were selected as model compounds of symmetrical conjugated dienes. 2-Methyl-1,3-butadiene and *trans*-1,3-pentadiene were taken as models of unsymmetrical conjugated dienes. These dienes were subjected to the standard monohydration procedure.

1,3-Cyclohexadiene was readily converted into the



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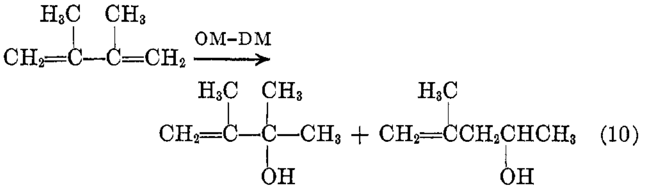
(9)

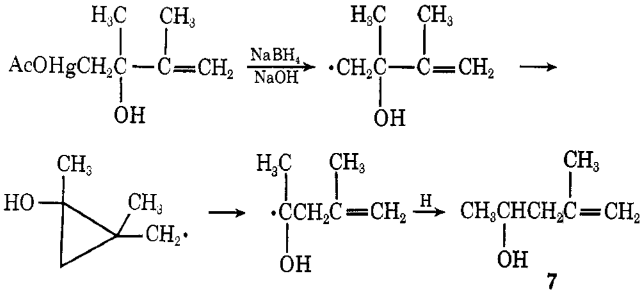
allylic derivative, 2-cyclohexen-1-ol (**5**), in 50% yield (eq 9), essentially the statistical value. We failed to observe the formation of the isomeric homoallylic alcohol, 3-cyclohexen-1-ol. This is in contrast to the report of Moon and coworkers,[14] who reported the formation of both isomers in equal amounts. However, the experimental conditions of this earlier investigation are not identical with those of the present study, so that a direct comparison of results may not be possible. Finally, it should be pointed out that the homoallylic alcohol is readily available *via* hydroboration of 1,4-cyclohexadiene with disiamylborane followed by oxidation with alkaline hydrogen peroxide.[5,6]

2,3-Dimethyl-1,3-butadiene undergoes reaction to provide a 49% yield of the expected product, 2,3-dimethyl-3-buten-2-ol (**6**), as well as 6% of a product, 4-methyl-4-penten-2-ol (**7**), containing a rearranged carbon structure (eq 10).



$$CH_2{=}\overset{H_3C}{\overset{|}{C}}{-}\overset{CH_3}{\overset{|}{C}}{=}CH_2 \xrightarrow{\text{OM-DM}} \underset{\mathbf{6}}{CH_2{=}\overset{H_3C}{\overset{|}{C}}{-}\underset{OH}{\underset{|}{\overset{CH_3}{\overset{|}{C}}}}{-}CH_3} + \underset{\mathbf{7}}{CH_2{=}\overset{H_3C}{\overset{|}{C}}CH_2\underset{OH}{\underset{|}{C}}HCH_3} \quad (10)$$

The results are consistent with an attack of mercury at the terminal position of the diene system, with addition of the nucleophile, water, to the adjacent position. We did not attempt to investigate the mechanism of the reaction responsible for the formation of the rearranged alcohol **7**. However, in view of the evidence that the demercuration step involves formation of a free radical,[10] the following mechanism appears reasonable (eq 11).



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(11)

The yield of the desired product from 2-methyl-1,3-butadiene was relatively low, only 16% of 2-methyl-3-buten-2-ol (**8**). There was also formed a small amount, 2%, of the isomeric enol, 3-methyl-3-buten-2-ol (**9**). The relative amounts of these two isomers correspond to expectations based on the relative reactivities of 2-methyl-1-pentene and 1-pentene.[11] There was also present 9% of a rearranged enol, 4-penten-2-ol (**10**) (eq 12). Presumably, the rearranged alcohol arises from the rearrangement of the intermediate free radical by changes similar to those shown in eq 11.

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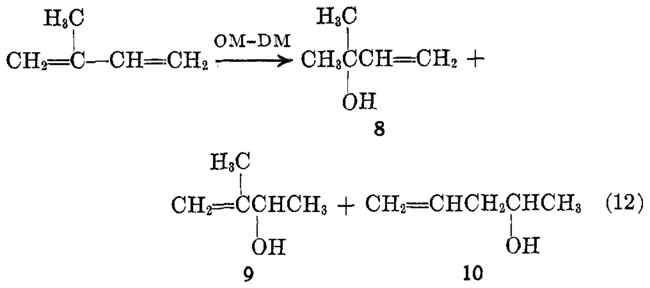
[14] S. Moon, J. M. Takakis, and B. H. Waxman, *J. Org. Chem.*, **34**, 2951 (1969).

TABLE V

MONOOXYMERCURATION–DEMERCURATION OF CONJUGATED DIENES

Diene	Temp, °C	Time, t_2,[a] hr	Yield,[b] %				
			Diene	$Enol_1$	$Enol_2$[c]	$Enol_3$[d]	Diol
1,3-Cyclohexadiene	0	0.5		50[e]	0[f]		16[g]
	0	1.0		48[e]	0[f]		19[g]
2,3-Dimethyl-1,3-butadiene	0	0.5	31	49[h]		6[i]	4[j]
2-Methyl-1,3-butadiene	0	2.6		16[k]	2[l]	9[m]	
trans-1,3-Pentadiene	0	1.0		56[n]			

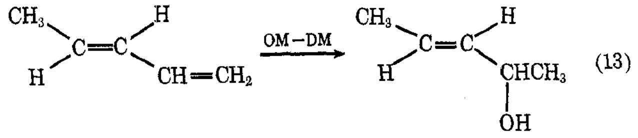
[a,b] See corresponding footnotes of Table I. [c] Isomeric enol. [d] Rearranged enol. [e] **5**. [f] 3-Cyclohexenol. [g] Diols similar to those produced in the dihydration of 1,3-cyclohexadiene by this method.[8] [h] **6**. [i] **7**. [j] Pinacol, plus 2% of other materials assumed to be diols from their retention times. [k] **8**. [l] **9**. [m] **10**. [n] **11**.



$$CH_2{=}\overset{\displaystyle H_3C}{\overset{|}{C}}{-}CH{=}CH_2 \xrightarrow{\text{OM-DM}} \underset{\mathbf{8}}{CH_3\overset{\displaystyle H_3C}{\overset{|}{\underset{\underset{\displaystyle OH}{|}}{C}}}CH{=}CH_2} + \underset{\mathbf{9}}{CH_2{=}\overset{\displaystyle H_3C}{\overset{|}{C}}\underset{\underset{\displaystyle OH}{|}}{C}HCH_3} + \underset{\mathbf{10}}{CH_2{=}CHCH_2\underset{\underset{\displaystyle OH}{|}}{C}HCH_3} \quad (12)$$

The low yields of enols from isoprene do not arise as a result of favored conversion to diol. A number of observations were made in the hope of understanding the basis for the low yield, but the problem was not resolved. The observations are reported in the Experimental Section.

Finally, *trans*-1,3-pentadiene is converted into *trans*-3-penten-2-ol (**11**) in 56% yield (eq 13). Consequently, here also attack occurs at the position predicted on the basis of the relative reactivities of 1-pentene and *trans*-2-pentene.



(13)

11

These results are summarized in Table V.

The applicability of mercuric trifluoroacetate for the monohydration of these conjugated dienes was also explored. However, the yields were uniformly poorer; so it is less favorable for this application than mercuric acetate.

Conclusion

The oxymercuration–demercuration procedure appears to provide a convenient general method for the monohydration of dienes. In the case of symmetrical nonconjugated dienes, yields approaching that possible for a statistical reaction, 50%, have been realized. Considerably higher yields are possible in unsymmetrical nonconjugated dienes, where the point of hydration is that double bond whose structural features correspond to a more reactive olefin. The method can be extended to many conjugated dienes, although in some cases the yields are lower owing to certain unusual behavior of the intermediates which is not yet understood.

Experimental Section

Materials.—All dienes used except 11-methyl-1,10-dodecadiene and 2-methyl-1,11-dodecadiene (preparation described below) were commercially available. Mercuric acetate, mercuric oxide, trifluoroacetic acid, and tetrahydrofuran were commercially available and used as obtained.

General Oxymercuration–Demercuration Procedure Using Mercuric Acetate.[15]—To a 100-ml flask equipped with a magnetic stirring bar were added 40 ml of tetrahydrofuran, 10 ml of water, and 10 mmol of diene. The solution was cooled to 0° with an ice–water bath and 10 mmol of mercuric acetate was added to the stirred solution. After an appropriate time interval (t_2) the reaction was completed by adding 10 ml of a 3 *M* NaOH solution followed by 10 ml of a 0.5 *M* $NaBH_4$ solution in 3 *M* NaOH. After stirring for an appropriate time (usually 0.5 hr) a suitable glpc standard was added and the aqueous phase was saturated with K_2CO_3. The upper layer was separated, dried over K_2CO_3, and analyzed by glpc using an appropriate column. In some cases, additional extraction of the aqueous phase was employed.

General Oxymercuration–Demercuration Procedure Using Mercuric Trifluoroacetate.—The procedure was identical with that used with mercuric acetate except that 10 mmol of mercuric oxide followed by 20 mmol of CF_3CO_2H was used in place of mercuric acetate.

Oxymercuration–Demercuration of 1,4-Pentadiene, 1,7-Octadiene, and 1,11-Dodecadiene.—The oxymercuration–demercuration procedure was described above. Identification of the enols from 1,4-pentadiene and 1,7-octadiene was made *via* ir and nmr by isolation of their acetates after acetylating the product from a large-scale preparation. The enol from 1,11-dodecadiene was identified by glpc *via* a mixed injection with an authentic sample of 11-dodecen-2-ol prepared by a published procedure.[16]

The diols listed in the text for these dienes are presumed to be those formed in the dihydration of the respective dienes.[8]

In addition to diene, enol, and diol, two additional components were observed from the 1,7-octadiene reactions using $Hg(O_2CCF_3)_2$. These two components were isolated by preparative glpc and their nmr spectra were recorded. Based on the nmr spectra we believe that the two components are the isomeric *cis*- and *trans*-2,7-dimethyloxepanes.

Preparation of 2-Methyl-11-dodecen-2-ol (1).—In a typical Grignard reaction, 0.358 mol of methyl-10-undecenoate in 40 ml of Et_2O was added to CH_3MgI prepared from 0.807 mol of Mg, 0.803 mol of CH_3I, and 200 ml of Et_2O. After the addition was complete, the solution was heated at reflux for 1.5 hr, cooled, and hydrolyzed with saturated NH_4Cl, and the ether layer was separated, dried (K_2CO_3), concentrated, and distilled, giving 60.9 g (86%) of **1**: bp 88–89° (0.6 mm) [lit.[17] bp 130° (10 mm)]; $n^{22}D$ 1.4491; ir (neat) 2.92, 3.21, 6.07, 10.06, 11.00, 13.85 μ; nmr (CCl_4) δ 5.8 (m, 1), 5.0 (m, 2), 2.0 (m, 2), 1.33 and 1.16 (m and s, 21).

Preparation of 11-Methyl-1,10-dodecadiene (12) and 2-Methyl-1,11-dodecadiene (13).—Using the general dehydration

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[15] The exact solvent system used varied between 75 and 85% aqueous THF and no significant difference in results was observed within this range.

[16] W. H. Urry, South African Patent 6,706,619 (1968); *Chem. Abstr.*, **70**, 87324a (1969).

[17] V. J. Harding, G. M. Walsh, and C. Weizmann, *J. Chem. Soc.*, **99**, 449 (1911).

method described,[18] 45.6 g of **1** was heated at 130° for 1 hr with 32 g of $(CO_2H)_2$ (oven dried, 110°, 3 hr). The product was taken up in Et_2O and filtered, and the ether phase was washed with $NaHCO_3$ solution, dried (K_2CO_3), concentrated, and distilled, giving 33.2 g (80%) of a mixture of **12** and **13**, bp 102–104° (8.5 mm) [lit.[19] for **12**, bp 94–95° (10 mm)], analyzing by glpc to be 72% **12**, 23% **13**, and 5% of presumably isomeric dienes. Fractionation of 15.5 g of the mixture was then carried out on a 24 mm × 1 m column containing 300 g of silica acid (60/200 mesh) impregnated with 20% $AgNO_3$, using pentane to elute **12**, followed by pentane/Et_2O mixtures to elute **13**. Fractions of desired purity (glpc) were combined and distilled over CaH_2 to give **12** [ir (neat) 3.24, 6.08, 10.08, 11.00, 12.0, 13.85 μ; nmr (CCl_4) δ 4.7–6.1 (m, 4), 1.98 (m, 4), 1.67 (s, 3), 1.58 (s, 3), 1.3 (m, 10)] and **13** [ir (neat) 3.22, 6.05, 10.08, 10.99, 11.28, 13.88 μ; nmr (CCl_4) δ 4.5–6.1 (m, 5), 1.97 (m, 4), 1.68 (s, 3), 1.32 (m, 12)].

Anal. Calcd for $C_{13}H_{24}$: C, 86.59; H, 13.41. Found for **13**: C, 86.45; H, 13.48.

Oxymercuration–Demercuration of 2-Methyl-1,11-dodecadiene (13).—Since 1 mmol of **13** with the standard 5 ml of 80% aqueous THF produced a two-phase system, an additional 1 ml of THF was used to achieve a homogeneous system before the mercuric salt was added. The enol isomer **1** arising from this diene was identified by glpc by mixed injection with a sample of **1** prepared by the Grignard method above. The other enol isomer was isolated by preparative glpc of the reaction of **13** with $Hg(O_2CCF_3)_2$ at 25° for 1 hr and identified as 11-methyl-11-dodecen-2-ol on the basis of the following spectral characteristics: ir (neat) 2.96, 3.21, 6.04, 11.23 μ; nmr (CCl_4) δ 4.67 (m, 2), 3.75 (m, 1), 2.0 (m, 2), 1.70 (approximately s, 3), 1.32 (m, 14), 1.11 (d, 3), 0.9 (s, 1). The diol **14** arising from **13** was identified by glpc by comparison with a sample whose preparation is described below.

Preparation of 2-Methyl-2,11-dodecanediol (14).—Oxymercuration–demercuration of **1** was performed according to the published method for unsaturated alcohols[8] except that $Hg(O_2CCF_3)_2$ was used instead of $Hg(OAc)_2$ and a 1-hr oxymercuration time was employed. The product was purified by sublimination at 90° (0.27 mm) to give **14**: mp 55–56°; ir (mineral oil mull) 2.95 μ; nmr ($CDCl_3$) δ 3.81 (m, 1), 1.50 (shoulder, OH by D_2O exchange), 1.33 (m), 1.21 (s), 1.18 (d, J = 7 Hz).

Anal. Calcd for $C_{13}H_{28}O_2$: C, 72.17; H, 13.04. Found: C, 72.29; H, 13.01.

Oxymercuration–Demercuration of 11-Methyl-1,10-dodecadiene (12).—Since 1 mmol of **12** with the standard 5 ml of 80% aqueous THF produced a two-phase system, an additional 1 ml of THF was used to achieve a homogeneous system before the mercuric salt was added. The minor enol product **1** was well as the diol product **14** arising from oxymercuration–demercuration of **12** were identified by glpc by comparison with authentic samples whose preparations have been described above.

The major enol product **2** was identified by isolation from a preparative reaction as follows. **12** (1.86 g) was oxymercurated–demercurated with 10 mmol of $Hg(O_2CCF_3)_2$ for 1 hr at 25° using 50 ml of THF and 10 ml of H_2O. Evaporation of the dried (K_2CO_3) layer gave a semisolid residue (the solid is probably salts of $CF_3CO_2^-$). The product was taken up in CH_2Cl_2 (the $CF_3CO_2^-$ salts are not as soluble in CH_2Cl_2) and chromatographed on alumina using pentane–Et_2O mixtures as eluent. Fractions analyzing (glpc) for >99% purity were combined and distilled to give **2**: bp 94° (0.5 mm); ir (neat) 2.95, 5.96, 11.95 μ; nmr (CCl_4) δ 5.05 (m, 1), 3.70 (m, 1), 1.88 (m, 2), 1.67 (s, 3), 1.58 (s, 3), 1.42 (s, 1, OH by D_2O exchange), 1.31 (m, 12), 1.12 (d, 3).

Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.79; H, 13.36.

Oxymercuration–Demercuration of Limonene (15).—The enol **3** arising from oxymercuration–demercuration of **15** was identified by comparison of glpc retention time with that of an authentic sample of α-terpineol. The diols arising from **15** were not identified but were presumed to be diols on the basis of glpc retention time.

Oxymercuration–Demercuration of 4-Vinylcyclohexene (16).—The major enol product **4** from oxymercuration–demercuration of **16** with $Hg(O_2CCF_3)_2$ for 1 hr at 25° was identified by isolation and comparison of its retention time and ir and nmr spectra with those of a sample of **4** produced by the reaction of 3-cyclohexene 1-carboxyaldehyde with methyl Grignard: bp 90–92° (18 mm); $n^{20}D$ 1.4836 [lit.[20] bp 93–93.5° (20 mm), $n^{20}D$ 1.4842]; nmr (CCl_4) δ 1.2 (d, 3), 1.8 (m, 7), 3.6 (m, 1), 4.2 (m, 1), 5.7 (s, 2). The minor components were assumed to be a mixture of bicyclic ethers since their retention times were shorter than those of the enol. Preparative glpc separation of this mixture yielded two components in the ratio of 5:1. Both have similar nmr spectra: δ 1.6 (m, 12), 4.2 (m, 2). The methyl doublet is shifted from δ 1.2 in the minor component to δ 1.0 in the major. Based on the recent work of Grubbs and coworkers, it is probable that these are the two 7-methyl-6-oxabicyclo[3.2.1]octanes.[21]

Oxymercuration–Demercuration of 1,3-Cyclohexadiene (17).—The enol **5** arising from oxymercuration–demercuration of **17** was identified by acetylating the evaporated THF extract with Ac_2O and pyridine and comparing glpc retention times with those of authentic samples kindly provided by Mr. P. Burke of 2-cyclohexen-1-yl acetate and 3-cyclohexen-1-yl acetate. None of the isomeric material could be detected. Components of long glpc retention time were presumed to be the diols found for dihydration of this diene.[8]

Oxymercuration–Demercuration of 2,3-Dimethyl-1,3-butadiene (18).—The enol **6** arising from **18** was identified by comparison of the nmr spectrum of a preparative glpc sample with that of an authentic sample prepared by a published procedure.[22] The rearranged enol **7** was identified only on the basis of the nmr spectrum of a preparative glpc sample: nmr (CCl_4) δ 1.15 (d, 3, J = 6 Hz), 1.55 (s, 1), 1.75 (d, 3, J = 1–2 Hz), 2.10 (d plus additional small splitting, 2, J = 6 Hz), 3.87 (sextet, 1, J = 6 Hz), 4.80 (m, 2). Pinacol was identified by glpc with an authentic sample.

Oxymercuration–Demercuration of 2-Methyl-1,3-butadiene (19).—The enols **8**, **9**, and **10** arising from **19** were identified by preparative glpc isolation followed by comparison of their ir and nmr spectra with those spectra of authentic samples of **8**, **9**, and **10** prepared as follows: **8** was prepared by the addition of CH_3Li to methyl vinyl ketone; **9** was prepared by the addition of CH_3Li to methacryladehyde; **10** was prepared by the published procedure.[23]

It should be noted that the **19** used in this study was distilled prior to use and gave only one peak upon glpc analysis under conditions which separated 1,4-pentadiene and *trans*-1,3-pentadiene from **19**. Thus the possibility that the rearranged enol **10** came from contamination of **19** with either of these isomeric dienes is excluded.

Another observation for the oxymercuration–demercuration of **19** was made; namely, that the Hg after reduction was not quantitatively found under the aqueous phase. Thus, 15 min after reduction the THF layer was separated, filtered repeatedly, and then evaporated on the rotary evaporator. Upon evaporation, 42% of the Hg was observed in the residue. This seems to indicate that dialkylmercurials, R_2Hg, are formed substantially in the reduction stage. Dialkylmercurials have previously been observed from $NaBH_4$ reductions of oxymercuration adducts under appropriate conditions.[10d] The presumed R_2Hg would then have to decompose slowly in THF upon standing or rapidly upon evaporation, since Hg precipitates under these conditions. Decomposition would presumably also occur during glpc analysis.[24] The glpc yields listed in the table may therefore be totally misleading with respect to the actual material present in solution. Nevertheless, they should be at least crude approximations to material isolated by normal thermal work-up. Similar considerations may also apply to the other conjugated dienes studied. At this time we have made no attempt to establish the factors responsible for this interesting and peculiar behavior, since it was beyond the scope of the objectives for this study.

Oxymercuration–Demercuration of *trans*-1,3-Pentadiene (20).—The enol **11** formed from the reaction of **20** was isolated by preparative glpc. Its ir spectrum was identical with that pub-

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[18] R. B. Carlin and D. A. Constantine, *J. Amer. Chem. Soc.*, **69**, 50 (1947).

[19] D. L. Christman and G. I. Keim, *Macromolecules*, **2**, 358 (1969).

[20] A. A. Petrov and N. P. Sopov, *Zh. Obshch. Khim.*, **22**, 591 (1952); *J. Gen. Chem. USSR*, **22**, 681 (1952).

[21] E. J. Grubbs, R. A. Froehlich, and H. Lathrop, *J. Org. Chem.*, **36**, 504 (1971).

[22] I. N. Rozhkov and S. M. Makin, *Zh. Obshch. Khim.*, **34**, 59 (1964); *J. Gen. Chem. USSR*, **34**, 57 (1964).

[23] W. H. Yanko, H. S. Mosher, and F. C. Whitmore, *J. Amer. Chem. Soc.*, **67**, 666 (1945).

[24] A review on dialkylmercurials has appeared: K. C. Bass, *Organometal. Chem. Rev.*, **1**, 391 (1966).

lished.[25] There was no absorption at 720 cm^{-1}, at which point the cis isomer absorbs strongly.

After reduction of the analytical run, only 55% of Hg was isolated. Addition of acid to the aqueous layer produced evolution of gas (presumably H_2) so that incomplete reduction was not due to insufficient hydride. During the preparative run, Hg was observed to emerge from the separated THF layer during work-up.

Registry No.—**1**, 34386-60-2; **2**, 34386-61-3; **4**, 17264-01-6; **7**, 2004-67-3; **12**, 18625-77-9; **13**, 34386-65-7; **14**, 34386-66-8; **15**, 138-86-3; **16**, 100-40-3; **17**, 592-57-4; **18**, 513-81-5; **19**, 78-79-5; **20**, 2004-70-8; mercuric acetate, 1600-27-7; 1,4-pentadiene, 591-93-5; 1,7-octadiene, 3710-30-3; 1,11-dodecadiene, 5876-87-9; mercuric trifluoroacetate, 13257-51-7; 11-methyl-11-dodecen-2-ol, 34386-69-1.

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[25] B. Heilmann, G. de Gaudemaris, and P. Arnaud, *Bull. Soc. Chim. Fr.*, 123 (1957).

Hydroxypropylation

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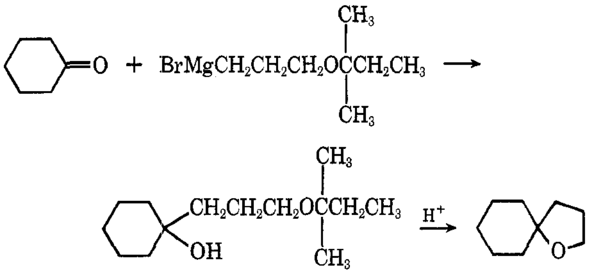
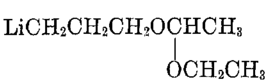
Organometallic reagents (**1**, **2**) useful in Grignard-type addition reactions are readily prepared from ethyl 3-bromopropyl acetaldehyde acetal (**3**). These reagents provide convenient means for the introduction of the hydroxypropyl group and the propionic acid chain.

We recently faced the problem of finding a convenient method for the introduction of the hydroxypropyl group, $-CH_2CH_2CH_2OH$, *via* organometallic-type reactions. Surprisingly, little in the literature is applicable to this problem. Grignard reagents from methyl,[1] ethyl,[2] and *tert*-amyl[3] ethers of 3-bromopropanol have been used in reactions with carbonyl compounds, but subsequent liberation of the primary hydroxyl group from its protecting ether mask cannot be accomplished readily without complication (*e.g.*, eq 1).[3]



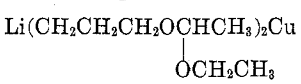
(1)

We report now our simple but exceedingly useful discovery that the organometallic reagents **1** and **2** are



$$LiCH_2CH_2CH_2OCH(OCH_2CH_3)CH_3$$

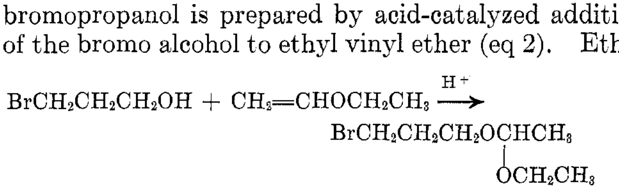
1



$$Li(CH_2CH_2CH_2OCH(OCH_2CH_3)CH_3)_2Cu$$

2

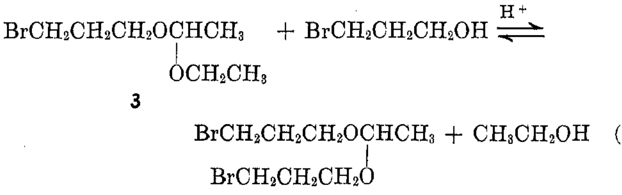
completely satisfactory carriers of the hydroxypropyl group. The parent of these reagents is ethyl 3-bromopropyl acetaldehyde acetal (**3**, alternate name, 1-ethoxyethyl 3-bromopropyl ether). This masked 3-bromopropanol is prepared by acid-catalyzed addition of the bromo alcohol to ethyl vinyl ether (eq 2). Ethyl vinyl ether was chosen for protection of the hydroxyl group rather than the more common reagent dihydropyran as (1) ethoxyethyl ethers are more readily removed by hydrolysis than the corresponding tetrahydropyranyl ethers,[4] and (2) the hydrolysis of an ethoxyethyl ether gives ethanol and acetaldehyde, both volatile and easily removed, whereas a tetrahydropyranyl ether gives the less convenient by-product 5-hydroxypentanal.



$$BrCH_2CH_2CH_2OH + CH_2{=}CHOCH_2CH_3 \xrightarrow{H^+} BrCH_2CH_2CH_2OCH(OCH_2CH_3)CH_3 \quad (2)$$

3

The reaction of 3-bromopropanol with ethyl vinyl ether is nearly quantitative and can be carried out readily on multimole scale if suitable care is exercised in the choice and use of the acid catalyst. Initially we used small amounts of methanesulfonic acid, but on too many occasions this led to explosive polymerization of the vinyl ether or, less disastrously, to production of the symmetrical acetal **4** *via* the exchange reaction shown in eq 3. We now employ dichloroacetic acid as the catalyst and avoid both these problems.



$$\underset{\mathbf{3}}{BrCH_2CH_2CH_2OCH(OCH_2CH_3)CH_3} + BrCH_2CH_2CH_2OH \overset{H^+}{\rightleftharpoons} \underset{\mathbf{4}}{BrCH_2CH_2CH_2OCH(OCH_2CH_2CH_2Br)CH_3} + CH_3CH_2OH \quad (3)$$

The lithium reagent **1** can be prepared on mole scale in ethyl ether as easily as a simple Grignard. The reaction of **3** with lithium wire (1% sodium) initiates spontaneously at room temperatures and continues rapidly below 0°.[5] One-molar solutions of **1** in ether are stable for months at −30°. Such solutions can be worked with unhurriedly at room temperature, but slow decomposition does occur to cyclopropane, among other things.

Addition of the lithium reagent **1** to a simple ketone is straightforward and proceeds in excellent yield. The product can be hydrolyzed to the primary alcohol *without* disturbing the nearby tertiary hydroxyl group, or

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[1] H. Erlenmeyer and R. Marbet, *Helv. Chim. Acta*, **29**, 1946 (1946). See also M. S. Kharasch and O. Reinmuth, "Grignard Reactions of Nonmetallic Substances," Prentice-Hall, Englewood Cliffs, N. J., 1954, p 36, and references cited therein.

[2] L. I. Smith and J. A. Sprung, U. S. Patent 2,421,090; *cf. Chem. Abstr.*, **41**, 5543 (1947).

[3] W. R. Renfrow, D. Oakes, C. Laver, and T. A. Walter, *J. Org. Chem.*, **26**, 935 (1961).

[4] S. Chladek and J. Smrt, *Chem. Ind.* (London), 1719 (1964).

[5] Oddly, the corresponding reaction with magnesium turnings does not proceed at all well in ether solvent. The Grignard can, however, be prepared in tetrahydrofuran. It is less useful than **1**.