Solvomercuration–Demercuration. I. The Oxymercuration–Demercuration of Representative Olefins in an Aqueous System. A Convenient Mild Procedure for the Markovnikov Hydration of the Carbon–Carbon Double Bond

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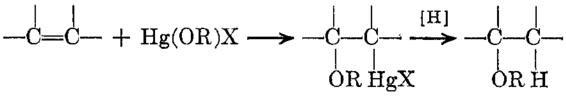
The reaction of olefins with mercuric acetate in aqueous tetrahydrofuran, followed by the *in situ* reduction of the mercurial intermediate by alkaline sodium borohydride, provides a highly convenient procedure for the Markovnikov hydration of the carbon–carbon double bond. The synthesis has been applied to a representative selection of olefins. It was observed that mono-, di-, tri-, and tetraalkyl, as well as phenyl-substituted olefins, undergo hydration readily by this procedure to give high yields of the Markovnikov alcohol, generally in excess of 90%. The reaction displays high specificity and sensitivity to steric factors, and advantage of these characteristics can be taken to achieve desired syntheses.

The hydroboration–oxidation of olefins provides a highly convenient procedure, without evident rearrangement, for achieving the anti-Markovnikov hydration of carbon–carbon double bonds.[3,4] For some time we had felt the need in our synthetic work for an equally mild procedure, equally free of rearrangement, for the Markovnikov hydration of carbon–carbon double bonds. Preliminary studies indicated that the oxymercuration of olefins in aqueous tetrahydrofuran, followed by *in situ* reduction of the organomercurial by alkaline sodium borohydride, offered great promise for this requirement.[5] Accordingly, we undertook a detailed study of the scope of this reaction. The results of that study are reported in the present paper.

It shortly became apparent that this convenient, combined procedure should be capable of very wide variation, and serve as a general technique for the introduction of a wide variety of nucleophiles to carbon–carbon double bonds in the Markovnikov direction. Thus, we have developed procedures for the synthesis of ethers[6] and amines,[7] and others have utilized the technique for the synthesis of alkyl azides[8] and peroxides.[9] Consequently, we have generalized our initial interest in oxymercuration–demercuration to solvomercuration–demercuration, and this more general interest is expressed in the title of this new series.

The oxymercuration reaction was originally explored by Hofmann and Sand, beginning in 1900.[10] Although an enormous number of studies of the reaction have appeared in the literature, these later papers have concerned themselves primarily with the mechanism of the reaction and the stereochemistry of the products.[11]

Stoichiometrically the oxymercuration reaction consists in the addition of a mercuric salt or of the elements of a mixed mercuric salt, Hg(OR)X, to an olefinic double bond. Reduction of the carbon–mercury bond (demercuration) gives the corresponding alcohol, ether, or ester.



$$-\overset{|}{C}=\overset{|}{C}- + \mathrm{Hg(OR)X} \longrightarrow -\underset{\mathrm{OR}}{\overset{|}{\underset{|}{C}}}-\underset{\mathrm{HgX}}{\overset{|}{\underset{|}{C}}}- \xrightarrow{[H]} -\underset{\mathrm{OR}}{\overset{|}{\underset{|}{C}}}-\underset{\mathrm{H}}{\overset{|}{\underset{|}{C}}}- \qquad (1)$$

At the time our systematic study was undertaken the usual procedure involved addition of a mercuric salt, HgX_2 (X = OAc, NO_3, ClO_4, etc.), or mercuric oxide and an acid (HNO_3, $HClO_4$, etc.) to an aqueous (R = H), alcoholic (R = alkyl), or acidic (R = acyl) solution of the olefin. The resulting mixture was stirred for times ranging from a few minutes to several days. Not infrequently, it was recommended that catalysts, such as strong acids,[12] peroxides,[12] boron trifluoride, etc., be used to enhance the rate.

It is puzzling why so many workers used such long reaction times. For example, Traylor and Baker[13] prepared norbornylmercuric acetate in 61% yield from the olefin by stirring the reagents (norbornene, mercuric oxide, and mercuric acetate) for 30 hr. In contrast, a reaction time of 30 sec was adequate to achieve a 100% yield in the conversion of norbornene to *exo*-norborneol by the present procedure.[14] Moreover, we have discovered that, not only are such long reaction times less convenient, but not infrequently they are actually deleterious and result in greatly decreased yields.

From the work of Hofmann and Sands, it is known that, in the case of simple olefins, the reaction proceeds in the Markovnikov sense (that is, by placing the mercury atom on the carbon atom having the more hydrogen) to give an almost quantitative yield of product. However, it has been reported that side reactions often interfere, leading to polymers,[11a] dialkylmercurials,[11a]

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[2] Graduate Research Assistant, 1968–1969, on a study supported by funds from the Esso Research and Engineering Co.

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

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

[5] H. C. Brown and P. J. Geoghegan, Jr., *J. Amer. Chem. Soc.*, **89**, 1522 (1967).

[6] H. C. Brown and M.-H. Rei, *ibid.*, **91**, 5646 (1969).

[7] H. C. Brown and J. T. Kurek, *ibid.*, **91**, 5647 (1969).

[8] C. H. Heathcock, *Angew. Chem.*, **81**, 148 (1969).

[9] D. H. Ballard, A. J. Bloodworth, and R. J. Bunce, *Chem. Commun.*, 815 (1969).

[10] K. A. Hofmann and J. Sand, *Chem. Ber.*, **33**, 1340 (1900), and subsequent papers.

[11] (a) For a thorough review of the literature through 1950, see J. Chatt, *Chem. Rev.*, **48**, 7 (1951). (b) Pertinent data on the stereochemical aspects of the reaction have been reviewed by N. S. Zefirov, *Usp. Khim*, **34**, 1272 (1965); *Russ. Chem. Rev.*, **34**, 527 (1965). (c) Various aspects of the reaction which have been explored since 1950 have been reviewed by W. Kitching, *Organometal. Chem. Rev.*, **3**, 61 (1968).

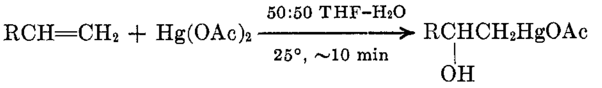
[12] J. Halpern and H. B. Tinker, *J. Amer. Chem. Soc.*, **89**, 6427 (1967), have studied the kinetics of hydroxymercuration in water and have shown that the rate is unaffected by acid concentration (over specified pH ranges) or by oxygen or hydroperoxide, contrary to some of these earlier reports and recommendations.

[13] T. G. Traylor and A. W. Baker, *ibid.*, **85**, 2746 (1963).

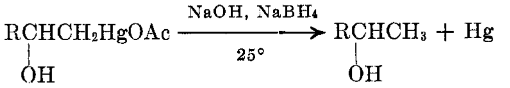
[14] H. C. Brown, J. H. Kawakami, and S. Ikegami, *ibid.*, **89**, 1525 (1967).

and products of oxidation[15] and substitution.[11a] Fortunately, these side reactions do not appear to be important under the conditions adopted for our hydration. Perhaps the much shorter reaction times utilized in our procedure contribute importantly in circumventing the appearance of these undesired side reactions.

Reduction of the carbon–mercury bond has been achieved using a number of reagents, including sodium–mercury amalgam, hydrazine, lithium aluminum hydride, and various borohydrides.[13,16,17] In practically all of the earlier work the initial oxymercuration product was precipitated as the chloride and this intermediate reduced in a separate operation. It was the recognition that oxymercuration could be accomplished very rapidly and essentially quantitatively in aqueous tetrahydrofuran (eq 2) and that the mercury could be removed *in situ* in a second fast reaction by treatment with alkaline sodium borohydride (eq 3) that persuaded us that this was the convenient Markovnikov hydration procedure that would complement the convenient anti-Markovnikov hydration procedure based on hydroboration–oxidation.



$$RCH{=}CH_2 + Hg(OAc)_2 \xrightarrow[25°,\ \sim 10\ min]{50:50\ THF-H_2O} \underset{\displaystyle OH}{RCHCH_2HgOAc} \quad (2)$$



$$\underset{\displaystyle OH}{RCHCH_2HgOAc} \xrightarrow[25°]{NaOH,\ NaBH_4} \underset{\displaystyle OH}{RCHCH_3} + Hg \quad (3)$$

Results and Discussion

It was our objective to develop a synthetic procedure for the Markovnikov hydration of the carbon–carbon double bond *via* oxymercuration–demercuration which would be simple in application and conducive to simple analysis and/or isolation of the products. The oxymercuration stage requires the addition of a water-soluble mercuric salt with a (generally) water-insoluble olefin. It is evident that a nucleophilic cosolvent might compete with water for the intermediate mercury species, giving a mixed product. Consequently, we chose a water–tetrahydrofuran (THF) solvent system in order to realize both the benefits of homogeneity (or near homogeneity) of the system and the inertness of the cosolvent.

Organomercuric salts are generally soluble, as the organomercuric hydroxides, in strongly alkaline solutions, and also quite stable in such solutions. Moreover, Bordwell and Douglass[16c] established that sodium borohydride reduces alkylmercuric salts or hydroxides both rapidly and smoothly in either neutral or alkaline solutions. In view of the greater solubility of the alkylmercuric hydroxide and the enormously greater stability of sodium borohydride in strongly alkaline solutions, we decided to utilize alkaline sodium borohydride for the *in situ* reduction. This worked ideally.

Mercuric acetate dissolves in water to give a clear solution. When 50 vol % of THF is added, a finely divided yellow precipitate appears. Presumably this is mercuric oxide or a basic mercuric acetate, although we have not attempted to establish the composition. Upon addition of the olefin this yellow precipitate or suspension disappears and a clear, colorless solution usually results, frequently in a matter of minutes or even seconds. In order to determine whether the time for disappearance of the yellow color (T_1) can be correlated to the extent of reaction, several olefins were oxymercurated and base was added immediately following the disappearance of the yellow color to stop further oxymercuration. The reaction mixture was then treated with sodium borohydride solution and analyzed for alcohol. The results are presented in Table I.

TABLE I

CORRELATION OF T_1 WITH EXTENT OF REACTION[a]

Olefin	T_1[b]	Yield of alcohol,[c] %
2-Methyl-2-butene	10 sec	61
Cyclohexene	55 sec	65
3,3-Dimethyl-1-butene	2 min	60
1-Dodecene	7 min	49

[a] Reaction run under standard conditions, as described in text. [b] Time for disappearance of the yellow color. [c] By glpc analysis. Markovnikov isomer only.

Some small variation in T_1 is observed from run to run, presumably because the reaction mixture is heterogeneous at the start of the reaction. However, the data indicate that the reaction has gone to approximately 60% of completion when all of the yellow precipitate or suspension has vanished. Although this may only be true for reactions carried out in a 1:1 THF–water solvent system, it should be approximately valid for other solvent ratios. In any event, the change in color provides a highly convenient, albeit approximate, measure of the reaction rate.

Using T_1 as an indication of the extent of reaction, the effect of solvent composition on the reaction was studied. 3,3-Dimethyl-1-butene (10 mmol) was added to the yellow suspension resulting from mixing 10 mmol of mercuric acetate and the volumes of water and THF indicated in Table II. The wide variation of T_1 with change in solvent composition demonstrates the desirability of selecting the proper solvent system to obtain optimum results.

TABLE II

THE EFFECT OF SOLVENT COMPOSITION ON THE RATE OF OXYMERCURATION OF 3,3-DIMETHYL-1-BUTENE

Vol of water, ml	Vol of THF, ml	T_1,[a] min
5	20	90
10	20	15
10	10	2
20	10	2
20	5	6

[a] Time for disappearance of the yellow color.

The effect of the THF to water ratio of the solvent system on the oxymercuration of 1-hexene and 1-octa-

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[15] (a) L. Balbiano and V. Paolini, *Chem. Ber.*, **35**, 2994 (1902); **36**, 3575 (1903). (b) K. B. Wiberg and S. D. Nelson, *J. Org. Chem.*, **29**, 3353 (1964). (c) Z. Rappoport, P. D. Sleezer, S. Winstein, and G. W. Young, *Tetrahedron Lett.*, 3719 (1965).

[16] (a) H. B. Henbest and B. Nicholls, *J. Chem. Soc.*, 227 (1959); (b) J. H. Robson and G. F. Wright, *Can. J. Chem.*, **38**, 21 (1960); (c) F. G. Bordwell and M. L. Douglass, *J. Amer. Chem. Soc.*, **88**, 993 (1966).

[17] For a more complete discussion, with pertinent references, see Bordwell and Douglass.[16c] The use of borohydrides for demercuration appears to have been introduced by Henbest and Nicholls,[16a] whereas Robson and Wright[16b] and Traylor and Baker[13] appear to have first used borohydride in aqueous solution for demercuration. However, we are indebted to Bordwell and Douglass[16c] for the first detailed study of such reductions in aqueous media and the recording of the great speed of that reaction.

decene was studied. The olefin, 10 mmol, was added to 10 mmol of mercuric acetate in 10 ml of water with either 10, 20, or 30 ml of THF. At the end of the appropriate interval of time, alkaline sodium borohydride was introduced to reduce the organomercurial. The variation of yield with time is given in Table III.

TABLE III
EFFECT OF THF TO WATER RATIO ON THE YIELD OF 2-HEXANOL AND 2-OCTADECANOL

Solvent composition, THF:H_2O	Time of reaction, hr	Yield of 2-hexanol, %	Yield of 2-octadecanol %
1:1	0.25	94	16
	1.0	95	48
	8.0	93	76
	24.0	96	93
2:1	0.25	92	82
	1.0	91	95
	8.0	93	92
	24.0	91	95
3:1	0.25	85	86
	1.0	83	93
	8.0	86	93
	24.0	90	96

From these results it is apparent that the reaction of the low molecular weight olefin, 1-hexene, is both rapid and quantitative. The yield of 2-hexanol is slightly lower in the 3:1 THF–water solvent system. The high molecular weight olefin, 1-octadecene, clearly shows the advantages of a less aqueous system in this case. The much slower reaction of 1-octadecene in the more aqueous solvents is presumably due to its very limited solubility in water and the more aqueous system.

In order to determine whether excess hydride is necessary for reduction, 10 mmol of 1-hexene was oxymercurated in a 1:1 THF–water (10 ml each) solvent system with 10 mmol of mercuric acetate. After 10 min, 10 ml of 3.0 *M* sodium hydroxide was added followed by various amounts of 0.5 *M* sodium borohydride in 3.0 *M* sodium hydroxide. The results (% excess H^-, % yield 2-hexanol: 10, 88; 50, 86; 100, 92) are essentially the same in all cases.

Another factor which may influence the yield is the temperature at which reduction takes place. Both styrene and 1-hexene were oxymercurated and base was added. The basic solutions were then either heated or cooled and borohydride solution (0.5 *M* sodium borohydride in 3.0 *M* sodium hydroxide, 100% excess) was added. The temperature was controlled during the addition. The yield of 2-hexanol varied between 88 and 95% with no trend observable. The results with styrene (Table IV) also show that the temperature of reduction is unimportant.

TABLE IV
EFFECT OF REDUCTION TEMPERATURE ON THE YIELD OF 1-PHENYLETHANOL

Reduction temp, °C	Yield of alcohol, %[a]	Reduction temp, °C	Yield of alcohol, %[a]
55–60	87	15–17	91
50–53	90	2–5	87
30–35	90	−5–0	91
32–35	89		

[a] Glpc analysis.

Mercuric salts, other than mercuric acetate, have also been used in the oxymercuration reaction. Mercuric nitrate and mercuric trifluoroacetate were allowed to react with several olefins in order to determine whether the anion had any pronounced effect on the reaction.

We explored the effect of the nature of the mercuric salt on the yield, using mercuric acetate, trifluoroacetate, and nitrate and a standard group of representative olefins. The results indicated that there was no significant change in the maximum yield with these salts. However, the yield dropped much more sharply with time in the case of the nitrate and the trifluoroacetate, especially with the more highly substituted olefins.[18] These results persuaded us that mercuric acetate would be most generally useful; so we adopted it for this study of the reaction scope.

With the above results in mind we designed a standard procedure for the oxymercuration–demercuration of olefins which is remarkable in its simplicity and speed.

In a 100-ml flask, fitted with a magnetic stirrer, is placed 3.19 g (10.0 mmol) of mercuric acetate. To this is added 10.0 ml of water (in which the salt dissolves), followed by 10.0 ml of THF. Then 10.0 mmol of 1-hexene is added. The reaction mixture is stirred for 15 min at room temperature (approximately 25°) to complete the oxymercuration stage. Then 10.0 ml of 3.0 *M* sodium hydroxide is added, followed by 10.0 ml of a solution of 0.50 *M* sodium borohydride in 3.0 *M* sodium hydroxide. Reduction of the mercurial is almost instantaneous. The mercury is allowed to settle. Sodium chloride or potassium carbonate is added to saturate the water layer. The upper layer of THF is separated—it contains an essentially quantitative yield of 2-hexanol, 94%.

We have encountered no serious difficulty in scaling the procedure up to runs on a preparative scale. However, it should be recognized that the reaction is exothermic, so that the rate of addition of base and basic hydride solutions should be controlled to maintain the temperature at approximately 25°.

As was pointed out previously the mercuric acetate originally dissolves in the water to give a clear solution. However, the addition of the THF forms a yellow precipitate. As the reaction proceeds, this coloration first becomes lighter and then the reaction mixture (usually) becomes colorless and clear (T_1), frequently in a matter of seconds, although in some cases, such as *trans*-4,4-dimethyl-2-pentene, longer periods are required. Although the oxymercuration reaction is not complete at this point, the disappearance of the yellow color provides an approximate indication of the time required. Usually we allowed the reaction to proceed for at least five to ten times the length of time required for the yellow color to vanish before initiating the reduction stage (T_2).

In considering the effect of olefin structure on the oxymercuration–demercuration reaction, it is advantageous to compare olefins with similar structural features. Consequently the data are presented individually for olefins of the following classes: I, monosubstituted terminal olefins, $RCH{=}CH_2$; II, disubstituted internal olefins, $RHC{=}CHR'$; III, disubstituted ter-

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[18] A detailed study of this phenomenon is underway with J. T. Kurek and the results will be reported shortly.

minal olefins, $R_2C{=}CH_2$; IV, trisubstituted internal olefins, $R_2C{=}CHR$; V, tetrasubstituted internal olefins, $R_2C{=}CR_2$. Unless otherwise stated, all of the following reactions were run under the above standard conditions.

Terminal Olefins, $RCH{=}CH_2$.—The data for this series of olefins is given in Table V. The reaction is rapid and clean leading to a quantitative conversion to alcohol. The olefins react within 15 min to give greater than 90% of the Markovnikov alcohol. As has been mentioned previously, the higher molecular weight olefins react more rapidly when a less aqueous system is used.

TABLE V

OXYMERCURATION–DEMERCURATION OF TERMINAL OLEFINS, $RCH{=}CH_2$

Olefin	T_1, sec	T_2, hr	Product	Yield, %[a]
1-Pentene	15	0.25	2-Pentanol	93
		1.0		97
1-Hexene	45	0.25	2-Hexanol	94
		1.0		95
1-Dodecene[b]		0.25	2-Dodecanol	91
		1.0		91
1-Octadecene[c]		0.25	2-Octadecanol	86
		1.0		93
3,3-Dimethyl-1-butene	120	0.25	3,3-Dimethyl-2-butanol	86
		1.0		94
Styrene	30	0.25	1-Phenylethanol	91
		1.0		90

[a] Glpc analysis. [b] THF : H_2O = 2:1. [c] THF : H_2O = 3:1.

Oxymercuration is known to proceed in the Markovnikov sense, that is, by placing mercury on the carbon atom which originally held the larger number of hydrogen atoms. The apparent homogeneity of the isolated mercurials, coupled with chemical determination of the positions occupied by –OR and –HgX, form the original experimental basis for this observation. Recently Kiefer and Waters have determined the nmr spectra of a number of isolated mercurials and have stated that the "methoxymercuration of all unsymmetrical olefins (which they studied) took place cleanly in the Markovnikov sense."[19]

We subjected the reaction mixtures obtained from 1-hexene, 3,3-dimethyl-1-butene, and 2-methyl-1-butene to careful glpc examination in order to determine quantitatively the purity of the Markovnikov alcohol formed in the reaction.

The product from 1-hexene revealed the presence of 0.5% of 1-hexanol on oxymercuration under our standard conditions. This alcohol was identified by its retention time. Addition of authentic 1-hexanol to the reaction mixture caused an appropriate increase in the size of the peak of this minor component.

Examination of the reaction mixture from 3,3-dimethyl-1-butene revealed a peak corresponding to 3% of the anti-Markovnikov alcohol product. Isolation of this material by preparative gas chromatography and comparison of its ir and nmr spectra and glpc retention time with those of an authentic sample identified it as 3,3-dimethyl-1-butanol.

There was less than 0.1% 2-methyl-1-butanol in the reaction mixture from 2-methyl-1-butene.

Thus the oxymercuration–demercuration reaction provides an extremely simple and quantitative method for Markovnikov hydration of monosubstituted olefins to give almost exclusively the desired isomer.

An examination of the glpc trace of the reaction mixture from oxymercuration of 3,3-dimethyl-1-butene failed to reveal the presence of any 2,3-dimethyl-2-butanol (<0.2%) which would be the product expected if the intermediate secondary carbonium ion were to rearrange to the tertiary ion. This lack of rearrangement is an important characteristic of the oxymercuration reaction.[11]

Disubstituted Internal Olefins, $RCH{=}CHR'$.—The yield of alcohols and percentage of 2-ols have been tabulated in Table VI. Here again the yield of alcohol from the various olefins is quantitative except for the somewhat lower yields for the propenylbenzenes.

This series of olefins brings out several important aspects of the oxymercuration–demercuration reaction. The first of these is that *cis* isomers react more rapidly than the corresponding *trans* olefins. This observation is based on the disappearance of the yellow precipitate (T_1). As partial confirmation of this is the observation that the yield of alcohol from *trans*-4,4-dimethyl-2-pentene is 52% after 6 hr, while the yield of alcohol from the corresponding *cis* isomer has reached 95% in 4 hr. This phenomenon has been noted previously,[20] and in one case its use in determining the configuration of isomeric olefins has been suggested.[20c]

The second aspect of this reaction that is evident from these data is the dramatic variation in rate of reaction with increased branching in the olefin. Taft has reported that the rate of hydration of olefins of the type $RC(CH_3){=}CH_2$ varies only slightly as R is changed from methyl (relative rate = 1.0) to ethyl (relative rate = 1.25) to *t*-butyl (relative rate = 1.0).[21] In contrast T_1 varies by a factor of about 500 from methyl to *t*-butyl in the oxymercuration of *trans*-$RCH{=}CHCH_3$. It thus appears that a rather large steric effect is operable in the oxymercuration–demercuration reaction. (The effect is smaller in the *cis* isomers.)

The distribution of the alcoholic OH group in the product between the two olefinic carbon atoms of the starting material also demonstrates the high susceptibility of this reaction to steric factors. The incoming OH group becomes attached preferentially to the least hindered carbon atom. The large preference of the OH group for the 2 position with increased inaccessibility of the 3 position is obvious from comparison of the relative amounts of 2-ol and 3-ol in either the *cis*- or the *trans*-4-substituted 2-pentenes (Table VI).

Herz and Gonzalez have recently reported that oxymercuration–demercuration of 5α-cholest-2-ene gives a 30:70 mixture of 2β- and 3α-cholestanols.[22]

Epoxidation of several 5α-cholest-2-enes has resulted in the formation of the α-epoxides, indicating that the α side is the least hindered side for such reactions.[23]

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[19] E. F. Kiefer and W. L. Waters, *J. Amer. Chem. Soc.*, **87**, 4401 (1965).

[20] (a) E. Biilmann, *Chem. Ber.*, **35**, 2571 (1902); (b) G. F. Wright, *J. Amer. Chem. Soc.*, **57**, 1993 (1935); (c) W. H. Brown and G. F. Wright, *ibid.*, **62**, 1991 (1940).

[21] R. W. Taft, ONR Report, 1960, p 6, as quoted in P.B.D. de la Mare and R. Boulton, "Electrophilic Additions to Unsaturated Systems," Elsevier Publishing Co., New York, N. Y., 1966, p 26.

[22] J. E. Herz and E. Gonzalez, *Ciencia* (Mexico City), **26**, 29 (1968); *Chem. Abstr.*, **69**, 36347*g* (1968).

[23] (a) C. Djerassi, N. Finch, R. C. Cookson, and C. W. Bird, *J. Amer. Chem. Soc.*, **82**, 5488 (1960); (b) J. F. McGhie, P. J. Palmer, and M. Rosenbarger, *Chem. Ind.* (London), 1221 (1959); (c) J. A. Zderic, M. E. C. Rivers, and D. L. Liman, *J. Amer. Chem. Soc.*, **82**, 6373 (1960).

TABLE VI

DISUBSTITUTED INTERNAL OLEFINS, RCH=CHR′

Olefin	Registry no.	T_1	T_2, hr	Yield of alcohol, %[a]	Isomers, % 2-ol[b]	Isomers, % 3-ol[c]
cis-2-Pentene	627-20-3	25 sec	0.25	93	64	36
trans-2-Pentene	646-04-8	50 sec	0.25	91	56	44
cis-4-Methyl-2-pentene	691-38-3	3 min	1.0	97	91	9
trans-4-Methyl-2-pentene	674-76-0	10 min	3.5	99	82	18
cis-4,4-Dimethyl-2-pentene	762-63-0	7 min	3.5	95	98	2
trans-4,4-Dimethyl-2-pentene	690-08-4	8 hr	16.0	91	95	5
cis-Propenylbenzene	166-90-5	45 min	24.0	77	88	12
trans-Propenylbenzene	873-66-5	5.5 hr	24.0	55	30[d]	70
Cyclopentene	142-29-0	20 sec	1.0	91		
Cyclohexene	110-83-8	55 sec	0.25	96		
Cyclooctene	931-88-4	2 hr	3.0	88		

[a] Total yield of both positional isomers. [b] $RCH_2CHOHCH_3$. [c] $RCHOHCH_2CH_3$. [d] Value at 15 min, yield approximately 5%. The per cent 2-ol gradually approaches that of the *cis* isomer.

TABLE VII

DISUBSTITUTED TERMINAL OLEFINS, $R_2C{=}CH_2$

Olefin	Registry no.	T_1	T_2, hr	Product	Yield, %[a]
2-Methyl-1-butene	563-46-2	10 sec	0.08	2-Methyl-1-butanol	90
			1.0		92
2,4,4-Trimethyl-1-pentene	107-39-1	3 min	0.30	2,4,4-Trimethyl-2-pentanol	87
Methylenecyclohexane	1192-37-6	10 sec	0.08	1-Methylcyclohexanol	99
α-Methylstyrene	98-83-9	45 sec	0.17	2-Phenyl-2-propanol	95

[a] Glpc analysis.

Attack by the mercuric salt (or ion) on the least hindered α side, followed by *trans* attack by water (diaxial addition) on the more hindered β side, would lead to the minor product. *trans*-Diaxial addition, initiated by mercury attack from the more hindered side, would give rise to the major product. Thus the product is apparently determined by the relative ease of attack by water on the intermediate.

The susceptibility of the oxymercuration–demercuration reaction to steric factors is indicated by these rather limited data.

Disubstituted Terminal Olefins, $R_2C{=}CH_2$.—These olefins can be oxymercurated to give quantitative yields of the corresponding tertiary alcohols in very short reaction times (Table VII). As mentioned previously, the reaction mixture from 2-methyl-1-butene was examined in order to determine the amount of anti-Markovnikov addition, but no 2-methyl-1-butanol could be detected.

Oxymercuration of 2,4,4-trimethyl-1-pentene proceeds smoothly to give an 87% yield of 2,4,4-trimethyl-2-pentanol in 18 min. Longer reaction times have a deleterious effect on the yield of alcohol. When the reaction is allowed to proceed for 8 hr, the yield of alcohol drops to 25%. After 24 hr, the yield is only 1% (Figure 1). In contrast the yield of 2-methyl-2-butanol from 2-methyl-2-butene remains at about 93% over a 24-hr period (Figure 1). Here again it appears as if a highly branched substituent has a profound effect on the course of the reaction.

Although the yield of alcohol in the case of 2,4,4-trimethyl-1-pentene is satisfactory, we have found that it is difficult to reproduce the maximum yield. This is primarily due to the sharp maximum and the heterogeneous nature of the initial stages of the reaction. This causes the reaction to proceed somewhat faster in some cases than in others, and makes it difficult to establish exactly when the maximum yield of alcohol has been attained.

In order to circumvent this difficulty, the reaction was run using 20 ml of THF for every 10 mmol of olefin (2:1 THF:H_2O). The maximum yield obtainable under these conditions was 71%. Increasing the amount of water to 20 ml/10 mmol of olefin (1:2 THF:H_2O) merely displaced the curve toward longer reaction times. The maximum yield (87%) was the same but the time required to obtain this maximum was slightly longer (~20 min).

The reaction was also carried out at 0–5°. In this case the yield of alcohol remained constant at the maximum (~87%) for a relatively long time (Figure 1). It thus appears as if the problem of undesirable side reactions (at least of the type observed here) for highly substituted olefins can be circumvented by running the reaction at somewhat lower temperatures.

Trisubstituted Internal Olefins, $R_2C{=}CHR$.—A wide variation in reactivity is displayed by olefins in this class, ranging from rapid and quantitative reaction for 2-methyl-1-butene to relative inertness for 1-phenylcyclopentene (Table VIII).

The behavior of 2-methyl-2-butene and 2,4,4-trimethyl-2-pentene is quite similar to that of the isomeric 1-olefins. The yield of 2-methyl-2-butanol from 2-methyl-2-butene reaches a maximum of 94% within 15 min and maintains this value for at least 24 hr (Figure 2). The yield of alcohol from 2,4,4-trimethyl-2-pentene reaches a maximum of about 70% in 0.5 hr and then decreases rapidly to 38% in 8 hr and 4% in 24 hr (Figure 2). When this olefin was oxymercurated at 0°, the yield of alcohol increased to 86% and was stable for several hours (Figure 2).

1-Phenylcyclopentene and 1-phenylcyclohexene are unreactive under our reaction conditions. Thus at the end of 4 hr the olefin is recovered unchanged.

TABLE VIII

TRISUBSTITUTED INTERNAL OLEFINS, $R_2C{=}CHR$

Olefin	Registry no.	T_1	T_2, hr	Product	Yield, %[a]
2-Methyl-2-butene	513-35-9	20 sec	0.25	2-Methyl-2-butanol	94
2,4,4-Trimethyl-2-pentene	107-40-4	30 min	1.5	2,4,4-Trimethyl-2-pentanol	72 (86)[b]
1-Methylcyclopentene	693-89-0	20 sec	0.10	1-Methylcyclopentanol	93
1-Methylcyclohexene	591-49-1	10 sec	0.08	1-Methylcyclohexanol	100
1-Phenylcyclopentene	825-54-7	>4 hr	4.0	1-Phenylcyclopentanol	0
1-Phenylcyclohexene	771-98-2	>4 hr	4.0	1-Phenylcyclohexanol	0

[a] Glpc analysis. [b] Reaction at 0°.

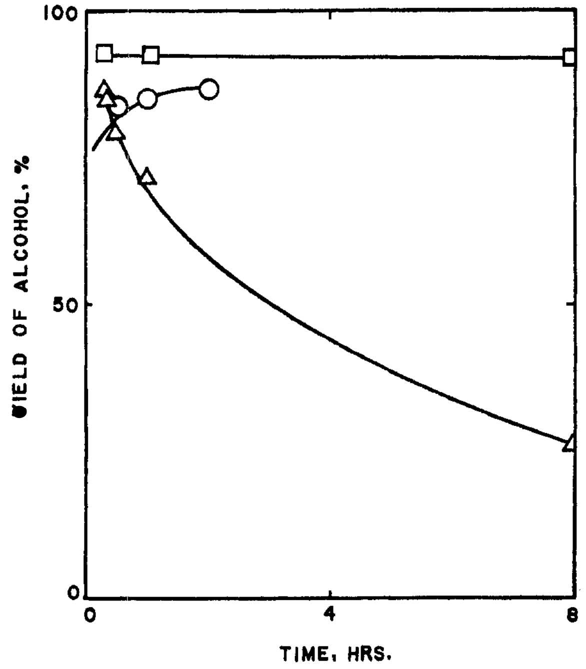

Figure 1.—Comparison of the yield of alcohol in the oxymercuration of 2,4,4-trimethyl-1-pentene at room temperature, △, and at 0°, ○, with that of 2-methyl-1-butene, □.

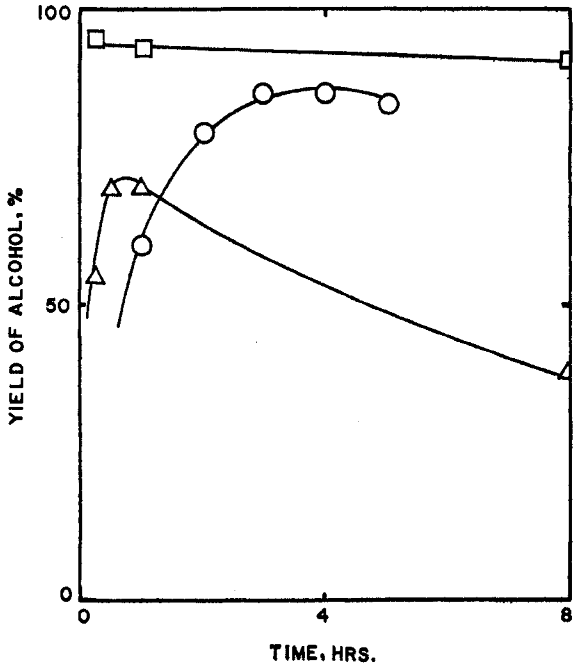

Figure 2.—Comparison of the oxymercuration of 2,4,4-trimethyl-2-pentene at room temperature, △, and at 0°, ○, with that of 2-methyl-2-butene, □.

When 1 mmol of mercuric acetate was allowed to react with 10 mmol of 1-phenylcyclohexene for 8 hr (10 ml of water, 10 ml of THF), the yellow color did not disappear indicating that the reaction had proceeded less than 10% in this length of time.

Tetrasubstituted Internal Olefins, $R_2C{=}CR_2$.—The only olefin of this class which we studied was 2,3-dimethyl-2-butene. Under our conditions 2,3-dimethyl-2-butanol is obtained in 85% yield in 15 min. As with the diisobutylenes previously discussed, the yield of alcohol decreases rapidly with time. After 8 hr, only 5% of the alcohol remains (Figure 3). Reaction at 0° slows the secondary reactions and increases the yield of alcohol slightly in this case also (Figure 3).

Investigation of the reaction mixture at the end of 8 hr clarified the course of the secondary reactions. The majority of the mercury was present as mercurous acetate, which precipitated from solution during the course of the reaction, and which was identified by comparison of its decomposition point (~270°) and ir spectra with that of an authentic sample of mercurous acetate.

There was 45% of the olefin and 5% of the tertiary alcohol. The products of oxidation were 2,3-dimethyl-2,3-butanediol (18%) and 3,3-dimethyl-2-butanone (17%). The latter compound was partially reduced under the reaction conditions to 3,3-dimethyl-2-butanol. The diol and the secondary alcohol were isolated and identified by comparison of their retention times and ir and nmr spectra with those of authentic compounds and with published spectra.

The products indicate that oxidation takes place by ionization of the tertiary mercurial to the tertiary carbonium ion,[24] which then rearranges to the ketone or reacts with water to form the diol.

Conclusion

The oxymercuration–demercuration sequence has been used to prepare the Markovnikov alcohol from a wide variety of olefins. It involves a simple procedure, easily applied. It appears to be of wide scope, applicable to a large number of structural types. 1-Phenylcyclopentene and -cyclohexene were the only olefins found to be unreactive. High molecular weight olefins react better in a less aqueous solvent, *i.e.*, one in which the proportion of THF has been increased. Highly branched (*e.g.*, diisobutylene-1 or -2) or highly sub-

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[24] F. R. Jensen and R. J. Ouellette, *J. Amer. Chem. Soc.*, **85**, 363, 367 (1963).

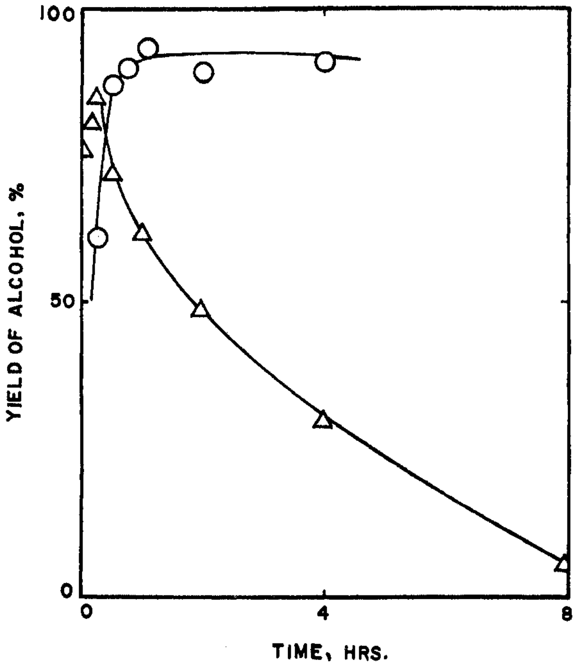

Figure 3.—Comparison of the oxymercuration of 2,3-dimethyl-2-butene at room temperature, Δ, and at 0°, O.

stituted (*e.g.*, tetramethylethylene) olefins are best run at 0° to minimize side reactions.

Experimental Section

Materials.—All olefins used were commercially available and were used as obtained unless glpc or index of refraction data indicated inpurities.

Mercuric acetate (Mallinckrodt Chemical Works), mercuric nitrate and mercuric oxide (J. T. Baker Chemical Co.), trifluoro acetic acid (3M Co.), sodium borohydride (Metal Hydrides, Inc.), and tetrahydrofuran (Fischer Scientific Co.) were used without further purification. Mercuric trifluoroacetate was prepared by a variation[6] of the method of Shearer and Wright.[25]

Oxymercuration Procedure.—The general procedure and various modifications have been discussed in appropriate places in the text.

Analysis.—The alcohol products were identified by comparison of gas chromatographic retention times with those of authentic samples of the alcohols. In several cases the products were isolated and compared with the known alcohols. Quantitative determinations were made by adding a suitable standard to the reaction mixture after reduction by borohydride. Calculations of yields were then made on the basis of relative thermal conductivities of standard and product as determined by integration of peaks obtained from a solution of standard and authentic alcohol. Analyses were carried out on either an F & M Model 300 chromatograph or a Perkin-Elmer Model 226 chromatograph. Integrations were obtained by using either a disk chart integrator or a Keuffel and Esser Co. planimeter.

Registry No.—1-Pentene, 109-67-1; 1-hexene, 592-41-6; 1-dodecene, 112-41-4; 1-octadecene, 112-88-9; 3,3-dimethyl-1-butene, 558-37-2; styrene, 100-42-5; 2,3-dimethyl-2-butene, 563-79-1.

[25] D. A. Shearer and G. F. Wright, *Can. J. Chem.*, **33**, 1002 (1955).

Factors Affecting Base-Induced Rearrangements of α-Chloro-α,α-diphenylacetamides

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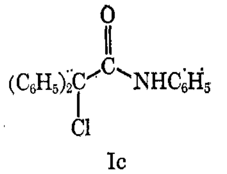
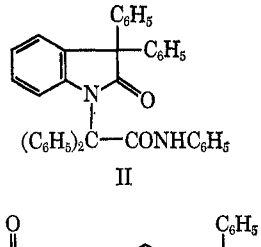
Effects of substituents and conditions on product distribution in reactions of N-substituted α-chloro-α,α-diphenylacetamides (Ia–Ie) with sodium amide in liquid ammonia, with liquid ammonia, and with aqueous ammonia are described. In liquid ammonia, in the presence or in the absence of sodium amide, the reaction leads to a product mixture consisting of two types of rearrangement products: (a) substituted ureas (VIIa and VIIb) and N-substituted α-amino amides (VIb–VIe), and (b) one displacement product (Va–Ve). These results are discussed in terms of a multistage process involving the intermediacy of a reactive α-lactam which undergoes two modes of ring opening. Formation of corresponding oxindoles (III) from the reactions of I in aqueous ammonia is also discussed.

Although α-chloro-α,α-diphenylacetanilide (Ic) was known since 1912,[1] a more systematic study of its chemistry has been realized only in the last decade. This development was induced by the endeavors aimed at synthesizing 1,3,3-triphenylaziridinone (α-lactam, IXc) from the reaction of Ic with strong bases.[2]

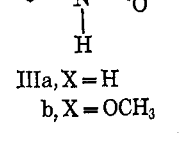
The reaction of Ic with sodium hydride in boiling benzene[3] was shown to yield a mixture of oxindole derivatives of structures II (predominant),[4] III (minor), and Ic (in minute quantities).[5] The formation of IXc as an intermediate was invoked to explain the Ic → II conversion.[4]



Ic

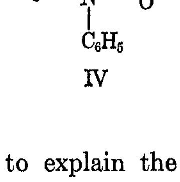


II



IIIa, X = H
b, X = OCH$_3$

IXc



IV

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[1] H. Klinger and G. Nickell, *Justus Liebigs Ann. Chem.*, **390**, 365 (1912).

[2] Endeavors aimed at synthesizing IXc from the reaction of Ic with strong base were unfruitful: (a) I. Lengyel and J. C. Sheehan, *Angew. Chem., Int. Ed. Engl.*, **7**, 25 (1968); (b) J. C. Sheehan and J. H. Beeson, *J. Amer. Chem. Soc.*, **89**, 366 (1967). (c) However, H. E. Baumgarten, R. D. Clark, L. S. Endres, L. D. Hagemeier, and V. J. Elia [*Tetrahedron Lett.*, 5033 (1967)] have reported that "1-*t*-butyl-3,3-diphenylaziridinone does not appear to be appreciably less stable thermally than the monophenyl α-lactam, 1-*t*-butyl-3-phenylaziridinone [H. E. Baumgarten, *et al.*, *J. Amer. Chem. Soc.*, **85**, 3303 (1963)], although it is *much more reactive chemically.*"

[3] S. Sarel and H. Leader, *ibid.*, **82**, 4752 (1960).

[4] S. Sarel, J. T. Klug, E. Breuer, and F. D'Angeli, *Tetrahedron Lett.*, 1553 (1964).

[5] J. C. Sheehan and S. W. Frankenfeld, *J. Amer. Chem. Soc.*, **83**, 4792 (1961).