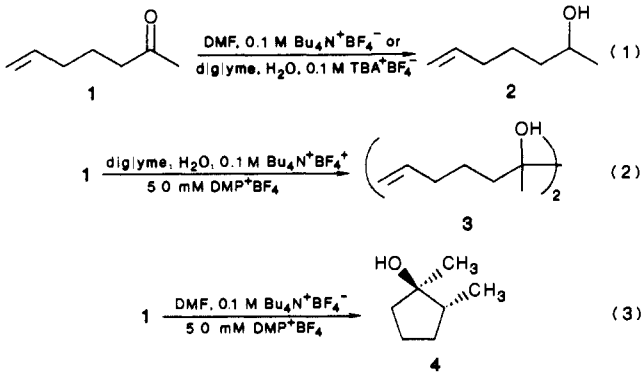
Electrochemical Reduction of Ketones Mediated by (Dimethylpyrrolidinio)mercury. Reductive Cyclization of Unsaturated Ketones and Redox Catalysis Studies

James E. Swartz,† Tendai J. Mahachi, and Essie Kariv-Miller*

Contribution from the Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455. *Received September 8, 1987*

Abstract: The mechanism of dimethylpyrrolidinium (DMP^+) mediation of the reductive cyclization of 6-hepten-2-one at a mercury electrode was studied. The initial step of the reduction involves formation of a solid composite, $(DMP)Hg_5$, which then transfers an electron to the ketone, regenerating DMP^+ and $Hg^•$. The ketyl radical anion cyclizes to form a primary alkyl radical, which can either abstract a hydrogen atom from the solvent, dimethylformamide, or be reduced to the corresponding carbanion. Protonation gives 1,2-dimethylcyclopentanol. Both direct and DMP^+-mediated reductions of 7-octen-2-one, 5-phenyl-2-pentanone, and 6-heptyn-2-one were studied. All three compounds give cyclic alcohols when the reduction is mediated by DMP^+. The former two compounds give the corresponding straight-chain alcohols when reduced directly. The latter gives the same cyclized product upon both direct or DMP^+-mediated reduction. Redox catalysis studies show that DMP^+ is a remarkably effective catalyst for the reduction of ketones. The effectiveness of the catalysis correlates with the expected rates of cyclization of the unsaturated ketones and is consistent with a mechanism involving mediation by solid $(DMP)Hg_5$. Redox catalysis studies of the reduction of cyclohexanones indicate that DMP^+-mediated reductions are accelerated by increasing $[H_2O]$, and the results are discussed in terms of a mechanism leading to pinacol formation.

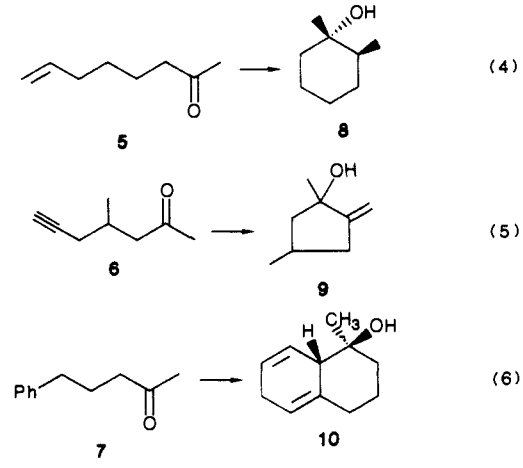
Reduction of 6-hepten-2-one (**1**) at mercury cathodes can result in the formation of a variety of products[1] (eq 1–3). Reduction in wet diglyme or in dimethylformamide (DMF) solution con-



taining 0.1 M tetrabutylammonium tetrafluoroborate ($Bu_4N^+BF_4^-$) consumes 2 faradays mol^{-1} and results in the formation 6-hepten-2-ol (**2**). Reduction of **1** in wet diglyme containing 0.1 M $Bu_4N^+BF_4^-$ and 5.0 mM dimethylpyrrolidinium tetrafluoroborate ($DMP^+BF_4^-$) consumes 1 faraday mol^{-1} and results in the formation of the pinacol **3**. Reduction of **1** in DMF containing 0.1 M $Bu_4N^+BF_4^-$ and 5.0 mM $DMP^+BF_4^-$ results in the formation of 1,2-dimethylcyclopentanol (**4**). Interestingly, the cyclic alcohol is formed almost exclusively as the cis isomer. A similar change from 1e to 2e products is seen for cyclohexanone, which forms cyclohexanol when reduced in $Bu_4N^+BF_4^-$-containing solvents but forms the corresponding pinacol (consuming 1 faraday mol^{-1}) when reduced in the presence of $DMP^+BF_4^-$. Reductions of **1** and cyclohexanone in the presence of $DMP^+BF_4^-$ readily occur 0.3–0.4 V positive of the potentials at which reduction can be carried out in its absence. At these potentials DMP^+ is reduced.

These results are consistent with the findings that reduction of tetraalkylammonium ions at mercury cathodes form insoluble mercury and tetraalkylammonium ion containing composites[2] that can in turn reduce a variety of difficult to reduce organic compounds.[3]

Shono and co-workers have also demonstrated the reductive cyclization of a series of unsaturated ketones at graphite or tin electrodes. They conducted preparative electrolyses of ketones at constant current in concentrated tetraethylammonium electrolyte solutions. In addition to 6-hepten-2-one (**1**), Shono has reported the following examples of reductive cyclizations (eq 4–6).



7-Octen-2-one (**5**) forms *cis*-1,2-dimethylcyclohexanol (**8**) in 75% yield when reduced at a graphite electrode in the presence of 2.0 M tetraethylammonium tosylate.[4] 4-Methyl-6-heptyn-2-one (**6**) gives the cyclic alcohol **9** when reduced under the same conditions.[5] 5-Phenyl-2-pentanone (**7**) gives the cyclic product **10** when reduced at a tin cathode in the presence of 2.0 M $Et_4N^+TsO^-$.[6] The reductive cyclization reactions are especially interesting in that they involve stereoselective ring formation. These syntheses required the consumption of 4–10 faradays mol^{-1}. Shono's work sheds no light upon the mechanism of these cyclizations or

† Present address: Department of Chemistry, Grinnell College, Grinnell, IA 50112-0806.

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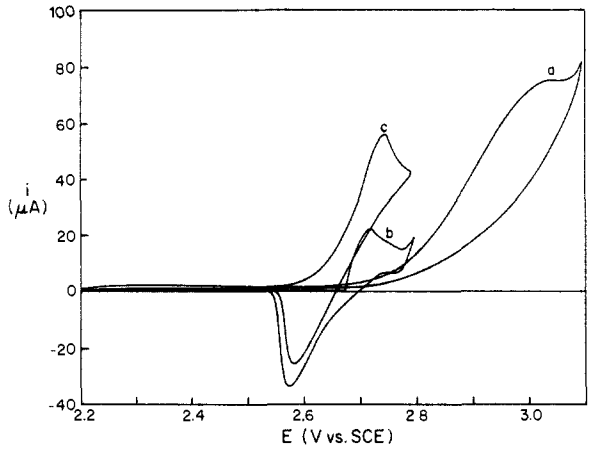


Figure 1. Cyclic voltammetry of the catalytic electroreduction of 6-heptyn-2-one (**11**) [0.10 M $Bu_4N^+BF_4^-$ in DMF, sessile hanging mercury drop electrode, 0 °C, 100 mV/s]: (a) 400 mM **11**; (b) 5.0 mM $DMP^+BF_4^-$; (c) a + b.

questions as to whether they involve mediation by reduced tetraalkylammonium composites of the electrode material.

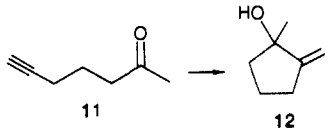
In this work we turn our attention to the scope of reductive cyclizations mediated by $(DMP)Hg_5$, the mechanism of DMP^+-mediated reduction of ketones, and the mechanism of the reductive cyclization of 6-hepten-2-one. We also report redox catalysis studies aimed at understanding the mechanism and kinetics of these reductions.

Results

Reductive Cyclization of 7-Octen-2-one (5), 5-Phenyl-2-pentanone (7), and 6-Heptyn-2-one (11). To test the generality of the DMP^+-mediated reductive cyclization of ketones, we examined the reduction reactions of the above compounds, 7-octen-2-one (**5**) to see whether 6- as well as 5-membered rings could be formed, 6-heptyn-2-one (**11**) to see whether alkynes could participate in reductive cyclizations, and 5-phenyl-2-pentanone (**7**) to see whether an aromatic ring could be involved in the cyclization.

Initial evidence for catalysis was obtained from cyclic voltammetric measurements. Cyclic voltammetry of **11** at a Hg electrode showed an irreversible reduction wave near the background of electrolyte decomposition (Figure 1). DMP^+ shows a reversible couple around −2.70 V, and the cathodic peak current of DMP^+ increased and the anodic peak current decreased upon addition of the ketone to a solution of 5.0 mM $DMP^+BF_4^-$. This evidence demonstrated that DMP^+ acts as a mediator for reduction of **11**. Behavior of **5** and **7** were similar, and more thorough cyclic voltammetric experiments will be presented later.

Armed with indications that DMP^+ could act as a mediator in the reduction of these ketones, we attempted preparative electrolyses, first in the absence of DMP^+ and then in its presence. Reduction of **5** at −3.00 V consumed 2 faradays mol^{-1} and resulted in the formation of a mixture of 7-octen-2-ol (45%) and **8** (35%). Reduction at −2.70 V in the presence of 5 mM $DMP^+BF_4^-$ gave **8** in 72% yield along with 10% of the corresponding pinacol, but no straight-chain alcohol was detected. Reduction of **7** at −3.00 V gave the expected 5-phenyl-2-pentanol in 80% yield along with the cyclized product **10**, in 10% yield. Reduction at −2.70 V in the presence of DMP^+ increased the yield of the cyclized product **10** to 80%, and no straight-chain alcohol was formed. Preparative reduction of **11** at −3.00 V resulted in the formation of the cyclized product **12** in 80% yield. None of the expected straight-chain alcohol, 6-heptyn-2-ol, was observed. Reduction of **11** at −2.70 V in the presence of DMP^+ gave **12** in an 85% yield (eq 7). The



11 12 (7)

fact that exclusive cyclization is observed for both the direct and

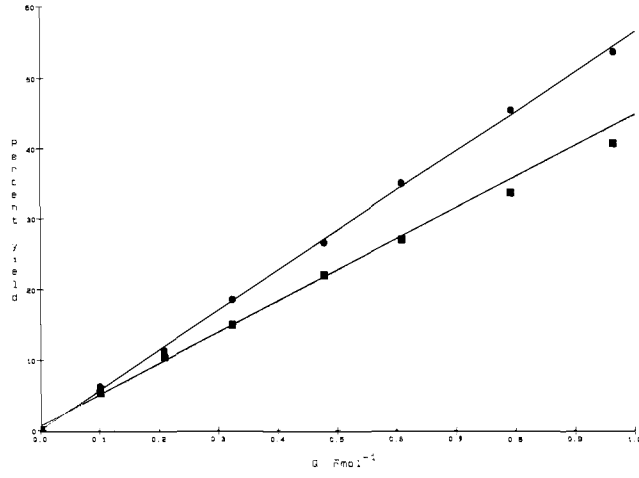


Figure 2. Electrolysis of 6-hepten-2-one (**1**). Percent yield vs number of electrons passed: ●, **1** reacted; ■, 1,2-dimethylcyclopentanol (**4**) formed.

DMP^+-mediated reductions indicates behavior differing from that of the other ketones. It is worthwhile to note that the terminal alkyne, 1-hexyne, showed no evidence of either direct or mediated reduction around −2.70 V, the potential region for DMP^+ reduction. A cyclic voltammogram of a solution containing 1-hexyne was identical with that of the solvent and electrolyte, alone. In addition, there was no change in the cathodic or anodic waves for DMP^+ when 1-hexyne was added to a solution of 5 mM DMP^+.

Cyclization of 6-Hepten-2-one (1). The following experiments were conducted to investigate the mechanism of the reductive cyclization of 6-hepten-2-one (**1**). Results of an experiment where, simultaneously, the consumption of charge and the product yields were measured are given in Figure 2. Experiments were conducted on a 40 mM solution of the ketone with 5.0 mM DMP^+ as a mediator. The yield of 1,2-dimethylcyclopentanol (**4**) increased and the amount of 6-hepten-2-one (**1**) decreased linearly with the amount of charge transferred. The linear plots indicate an overall stoichiometry of 2 electrons/ketone reacted. (The lack of coincidence of the points representing the amount of ketone reacted and the amount of cyclic alcohol formed are due to mass balances being somewhat less than 100%. The mass balance steadily decreased from 99% to 87% as the reaction progressed, and we believe this is due to problems with our analytical method rather than to some interesting chemistry.[7])

Reduction of **1** mediated by DMP^+ in DMF-d_7 solvent resulted in the quantitative formation of the cyclic alcohol **4**. Mass spectral analysis of products after passing 1 faraday mol^{-1} indicated that 30% of **4** was monodeuteriated and the remaining **4** was undeuteriated.

A series of electrolyses were conducted in the presence of increasing amounts of water (Table I). The addition of water had essentially no effect upon either the amount of cyclic alcohol formed or the stereochemistry of the cyclization.

Polarographic Measurements of DMP^+-Mediated Reduction of Cyclohexanones. Previous work has shown that DMP^+ catalyzed the reduction of cyclohexanone[1] and methylcyclohexanones[9] and lead to the formation of pinacols as products. Since the DMP^+-mediated reduction of cyclohexanones consumed only 1 faraday mol^{-1} and formed pinacols (products requiring only 1 faraday mol^{-1}) and nonmediated reduction consumed 2 faraday mol^{-1} and formed cyclohexanols, we decided to study the mech-

(7) When aliquots were removed from the reaction mixture and exposed to air, a brown color was observed. Oxidation of ketones by O_2 in the presence of alkoxide ions has been reported.[8] We attempted to minimize exposure to air of aliquots withdrawn in this experiment. It is worthwhile to note that since the reaction consumes 2 mol of H^+/mol of **4** formed, the reaction mixtures get progressively more basic.

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Table I. Effect of Added Water[a] on Dimethylpyrrolidinium-Mediated Reductions of 6-Hepten-2-one (**1**)

$[H_2O]$	1, %	4, %	4 (cis/cis + trans)
0[b]	29	53	0.95
0.10	36	48	0.92
0.50	30	57	0.95

[a] Electrolysis conducted in DMF on 40 mM 6-hepten-2-one, 5 mM DMP^+, 0.1 M $TBA^+BF_4^-$, 0 °C. 1.0 faraday mol^{-1} of ketone was passed at −2.70 V. Yields were determined by gas chromatography. <1% pinacol was detected in any reactions. [b] Burdick and Jackson DMF distilled and stored over activated alumina.

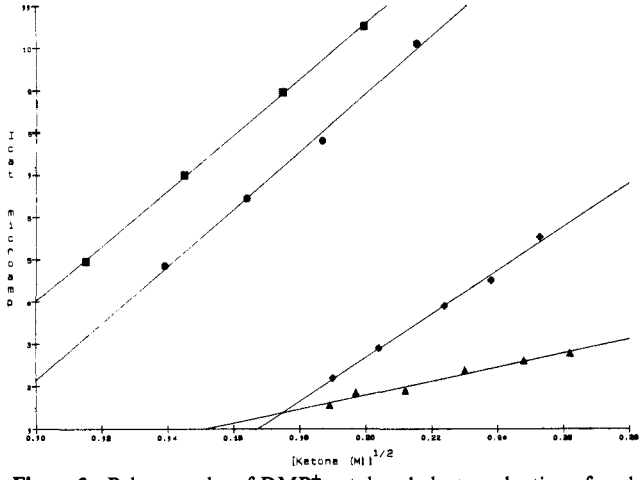


Figure 3. Polarography of DMP^+-catalyzed electroreduction of cyclohexanones. Catalytic current (I_c) vs [ketone]$^{1/2}$ [0.1 M $Bu_4N^+BF_4^-$ in DMF (0.30 M H_2O for methylcyclohexanones), 0 °C, 0.5-s drop time]: cyclohexanone; ●, 2-methylcyclohexanone; ▲, 3-methylcyclohexanone; ♦, 4-methylcyclohexanone.

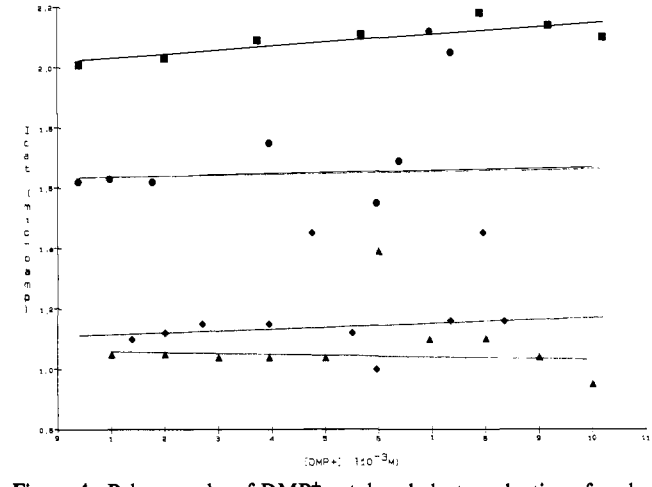


Figure 4. Polarography of DMP^+-catalyzed electroreduction of cyclohexanones. Catalytic current vs [DMP^+] [0.10 M $Bu_4N^+BF_4^-$, 0.30 M H_2O, 20 mM ketone in DMF at 0 °C, 0.5-s drop time]: ■, cyclohexanone; ●, 2-methylcyclohexanone; ▲, 3-methylcyclohexanone; ♦, 4-methylcyclohexanone.

anism of this reaction in more detail. We report here polarographic studies of this catalysis.

DMP^+ exhibits a polarographic wave with $E_{1/2} = -2.70$ V. The cyclohexanones did not exhibit any cathodic current in this region but did give significant currents near the solvent discharge background. When cyclohexanone was added to a DMP^+ solution, the limiting current for DMP^+ increased significantly, indicating catalysis. Similar behavior was exhibited by 2-, 3-, and 4-methylcyclohexanones, but the catalytic effect was more pronounced in the presence of water.

The catalytic current, I_c (the limiting current for the ketone plus DMP^+ less the limiting current for DMP^+ alone), varied linearly with the square root of the [ketone] (Figure 3) but was

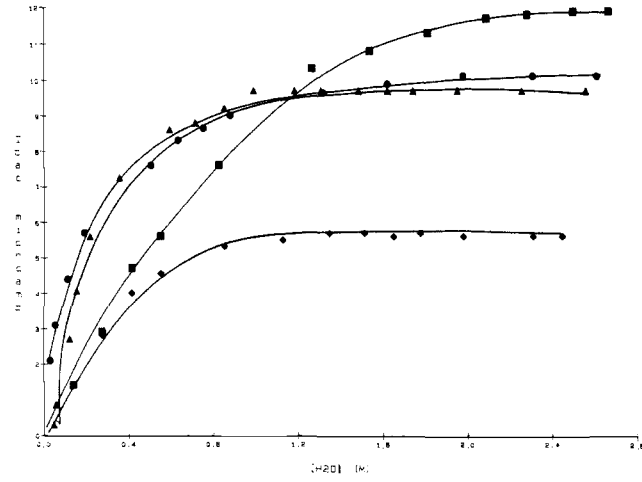


Figure 5. Polarography of DMP^+-catalyzed electroreduction of cyclohexanones. Catalytic current (I_c) vs [H_2O] [0.10 M $Bu_4N^+BF_4^-$, 2.0 mM $DMP^+BF_4^-$, 10 mM ketone in DMF at 0 °C, 0.5-s drop time]: ■, cyclohexanone; ●, 2-methylcyclohexanone; ▲, 3-methylcyclohexanone; ♦, 4-methylcyclohexanone.

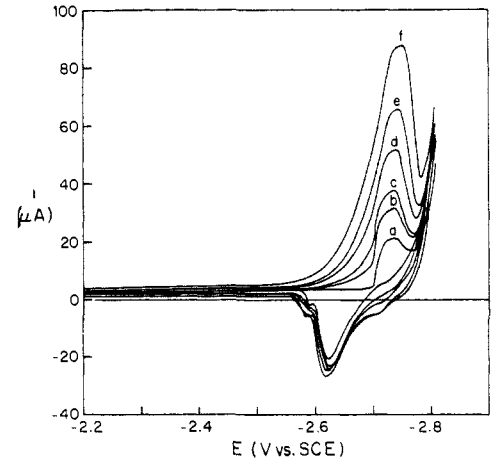


Figure 6. Cyclic voltammetry of DMP^+-catalyzed electroreduction of 6-hepten-2-one (**1**). [**1**] × 10^3 [0.10 M $Bu_4N^+BF_4^-$ and 2.0 mM $DMP^+BF_4^-$ in DMF at 0 °C, sessile hanging mercury drop electrode, 100 mV/s]: (a) 0, (b) 2.0, (c) 4.0, (d) 8.0, (e) 12.0, (f) 18.0.

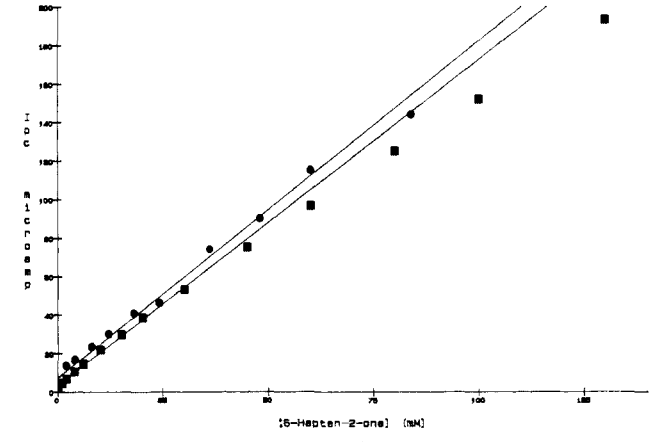


Figure 7. Cyclic voltammetry of $DMP^+BF_4^-$-catalyzed electroreduction of 6-hepten-2-one (**1**). Cathodic peak current vs [**1**] [0.10 M Bu_4N^+ BF_4^- in DMF at 0 °C, sessile hanging mercury drop electrode, 100 mV/s]: ●, [$DMP^+BF_4^-$] = 2.0 mM; ■, [$DMP^+BF_4^-$] = 0.75 mM.

nearly invariant with the [DMP^+] (Figure 4). For all four ketones the addition of water resulted in an increase in the catalytic current up to a limiting plateau Figure 5).

Cyclic Voltammetry of DMP^+-Mediated Reductions of Unsaturated Ketones. We decided to study the catalysis by DMP^+

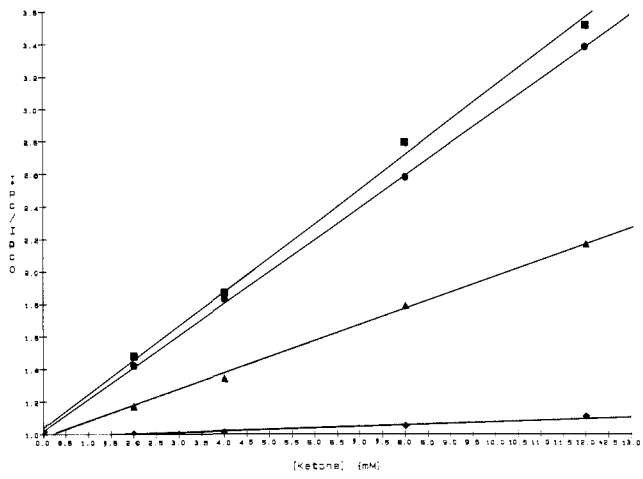


Figure 8. Cyclic voltammetry of $DMP^+BF_4^-$-catalyzed electroreduction of unsaturated ketones. Cathodic peak current vs [ketone] [0.10 M $Bu_4N^+BF_4^-$ and 2.0 mM $DMP^+BF_4^-$ in DMF at 0 °C, sessile hanging mercury drop electrode, 100 mV/s]: ■, 6-hepten-2-one (**1**); ●, 6-heptyn-2-one (**11**); ▲, 7-octen-2-one, (**5**); ♦, 5-phenyl-2-pentanone (**7**).

of unsaturated ketone reductions in more depth. Figure 6 presents cyclic voltammograms of DMP^+ in the presence of varying amounts of 6-hepten-2-one (**1**). As more ketone was added, the cathodic peak current increased and the shape of the wave, especially the initial portion of the cathodic wave, changed. Figure 7 presents a plot of the cathodic peak current, I_{pc}, for the DMP^+ peak vs [6-hepten-2-one] for two different [DMP^+]. I_{pc} increased with increasing [ketone], the increase up to 30 mM [ketone] being linear. The peak current response at 0.75 mM DMP^+ is parallel to that at 2.0 mM DMP^+. Note that the peak current for 0.75 mM DMP^+ was 3.0 μA in the absence of ketone. In the presence of 130 mM 6-hepten-2-one the peak current increased by a factor of 64 (to 193 μA)!

The three other unsaturated ketones, **5**, **7**, and **11**, behaved similarly. Figure 8 shows a plot of I_{pc}/I_{pc}^0 (the cathodic peak current in the presence of ketone, I_{pc}, divided by the cathodic peak current for DMP^+ alone, I_{pc}^0) vs [ketone]. The peak current response is linear with [ketone]. The slopes of those lines (**1**, 210 M^{-1}; **11**, 197 M^{-1}; **5**, 99 M^{-1}; **7**, 9.4 M^{-1}), however, vary significantly with the structure of the ketone, 6-hepten-2-one (**1**) giving rise to the highest currents, followed by 6-heptyn-2-one (**11**), 7-octen-2-one (**5**), and 5-phenyl-2-pentanone (**7**). The slope of the line for **1** is 20 times that for **7**.

Discussion

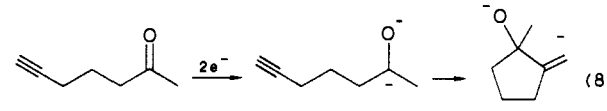
Reductive Cyclization of 5, 7, and 11. Like compound **1**, the DMP^+-mediated reductions at −2.70 V of **5**, **7**, and **11** give cyclic alcohols. With **5** and **7**, just as with **1**, the major product of direct reduction at −3.00 V is the straight-chain alcohol. We do not fully understand the effect of DMP^+ mediation on the course of these reductions, but it may be that a ketyl radical anion is formed in both the mediated and direct reductions. In the case of the mercury electrode at −3.00 V, a second electron is transferred (perhaps subsequent to protonation) giving the alcohol. In the case of DMP^+ mediation, however, the reducing agent, $(DMP)Hg_5$, has a substantially more positive reduction potential and does not rapidly reduce the ketyl radical anion, but the ketyl attacks the respective olefinic or aromatic bond. Compounds **5** and **7** do differ from **1** in that some cyclic products are formed even in the direct reductions. Apparently cyclization competes with reduction of the ketyl more effectively than in the case of **1** (where no cyclic alcohol is detected in direct reduction experiments).

The cyclization of **7** is remarkable in that it involves attack of a radical onto an aromatic ring. Such radical cyclizations onto aromatic rings are unusual but have been previously observed.[6,10] They could be important from both mechanistic and preparative viewpoints. These electroreductions, similar to that of **1**, give stereospecific cyclic alcohols. In the case of **5** and **7**, attack of the ketyl on the carbon–carbon π occurs such that the OH group ends up cis to the hydrogen (the methyl group cis to the alkyl group). Such stereochemical preferences have been observed previously in radical cyclizations and have been rationalized on the basis of stereoelectronic effects[11] and molecular mechanics calculations.[12]

The reduction of 6-heptyn-2-one (**11**) is different. Reduction in both the presence and absence of DMP^+ gives the same, cyclic, product. Since direct reduction of **11**, unlike direct reduction of the other ketones, gives only cyclized product, we wondered whether the mechanism of formation of cyclic product might be fundamentally different. One alternative pathway would be initial reduction of the alkyne, followed by addition of the radical anion (localized on the alkyne) to the carbonyl. We are spurred to consider this pathway in light of recent reports of the rapid intramolecular addition of aliphatic radicals to carbonyl groups.[13] To test this hypothesis, we examined the reduction of a terminal alkyne, 1-hexyne. Cyclic voltammetry indicated that 1-hexyne could not be reduced at this potential range either by direct means or by DMP^+ mediation. These results indicate that reduction of the alkyne cannot be the initial step in the mechanism and allows us to discard mechanisms invoking such a step.

Another possible explanation for the formation of the cyclic alcohol under direct electrolysis may be that the cyclization reaction (analogous to step M3) is faster with the 6-heptyn-2-one than with 6-hepten-2-one. If cyclization occurred more rapidly than reduction of the ketyl, cyclic alcohol would form rather than straight-chain alcohol.

Yet another explanation is that, under electrolysis at −3.00 V, the dianion is formed and that dianion undergoes an ionic intramolecular cyclization (eq 8). In order for this mechanism to



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pertain, the rate of cyclization would have to exceed the rate of protonation on carbon. This type of behavior is not demonstrated for the reduction of the other three ketones, but nucleophilic addition to alkynes is substantially more rapid than to alkenes or unsubstituted aromatic rings.[14]

Mechanism of Reductive Cyclization of 6-Hepten-2-one (1). Two reasonable mechanisms for the reductive cyclization of 6-hepten-2-one (**1**) are sketched in Scheme I.

The logical first steps in the DMP^+-mediated reductive cyclization reaction are the formation of $(DMP)Hg_5$ followed by electron transfer to the ketone, forming the ketyl radical ion (steps M1 and M2). Intramolecular reaction of ketyl radicals with carbon–carbon double bonds is precedented in both electrochemical[4-6] and metal reduction literature,[15] and we have discussed the stereochemistry of step M3 elsewhere.[1] After cyclization we are left with a molecule, $R_2^{\cdot -}$, that is both an alkoxide ion and a primary alkyl radical. Since reduction potentials of primary alkyl radicals have been estimated to be more positive than −2.30 V,[16] that radical should be readily reduced by the electrode, $(DMP)Hg_5$, or a ketyl radical anion. The β-alkoxy substituent might make that primary radical more difficult to reduce than an unsubstituted primary radical, but that substituent effect is

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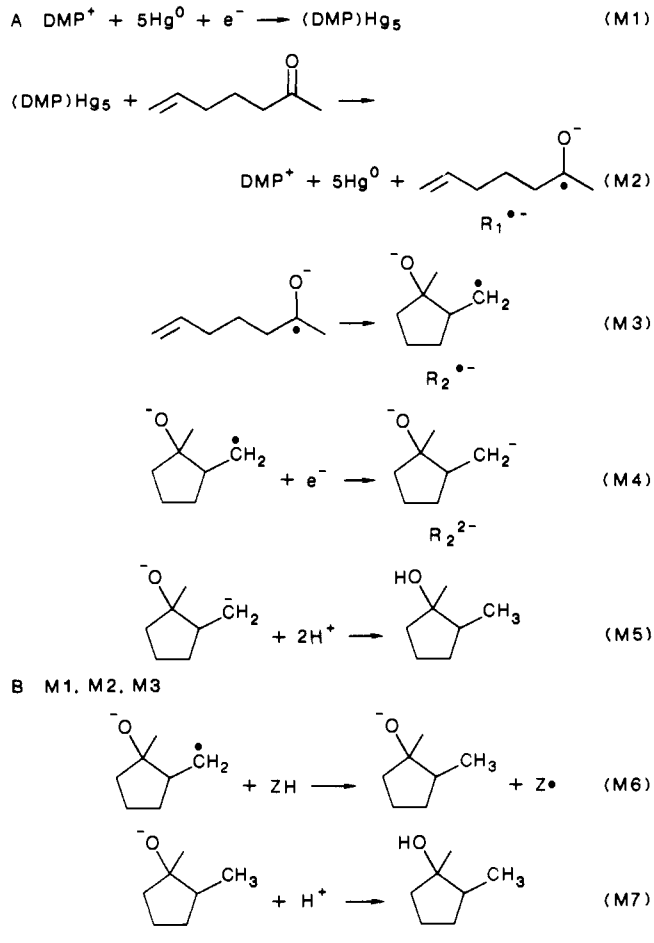
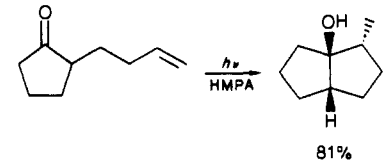
Scheme I



unlikely to overcome the exergonicity ($\geq$0.4 V)[2d] of this reaction in the absence of the alkoxy substituent. The primary alkyl radical may also abstract a hydrogen atom (pathway B) from the solvent, or other hydrogen atom donor, to form the observed product. Dimethylformamide has been previously found to serve as a hydrogen atom donor for alkyl and aryl radicals, and other components of the electrolysis medium are less likely hydrogen atom donors.[17]

An alternate pathway might invoke protonation of the ketyl radical anion prior to cyclization. The pK_a of the ketyl derived from acetone, $(CH_3)_2\dot{C}OH$, is about 12 in water.[18] This indicates that protonation of $R_1^{\bullet -}$ is disfavored by 3–4 pK units. The difference in pK_a's (between H_2O and the ketyl) in DMF is likely to be greater than 3–4 that since the lack of solvation of anions is likely to disfavor the deprotonation of water, more than the deprotonation of the ketyl which gives a delocalized anion. There is a report in the literature that cyclization of the protonated ketyl gives nearly equal mixtures of *cis*- and *trans*-1,2-dimethylcyclopentanols.[19] If protonation were occurring in our reaction, we would expect to observe some effect on the stereochemistry of the product when the water concentration was increased from very low ("dry solvent") to 0.5 M. No such effect was observed, which leads us to prefer mechanisms involving protonation subsequent to cyclization.[20]

Photochemical cyclization of unsaturated ketones similar to 6-hepten-2-one has been reported to give products with the hydroxyl group trans to the methyl group almost exclusively.[21] For instance, irradiation of 2-(4-butenyl)cyclopentanone gives a single isomer of the bicyclic alcohol (eq 9).[21b] The mechanism for these



(9)

81%

reactions, which are conducted in aprotic solvents, is thought to involve cyclization of the ketyl radical anion as in step M3. The fact that the stereoselectivity of the reactions reported here is the same as the photochemical reactions provides further support for our assertion that it is the ketyl radical anion, not the protonated ketyl that cyclizes.

The fact that ketyl radicals that are photogenerated[21] and electrogenerated (at different cathode materials)[4-6] give similar cyclized products is supportive of our mechanism that does not involve Hg, DMP^+, or $(DMP)Hg_5$ subsequent to the formation of the ketyl (step M2). Occum's razor encourages us to discard mechanisms involving DMP^+- or Hg-containing species subsequent to step M2.

Pathway A requires the consumption of 2 faradays mol^{-1} of ketone while pathway B requires only 1 faraday mol^{-1} of ketone. Pathway B may consume 2 faradays mol^{-1}, however, if the resultant radical, Z•, is subsequently reduced. Examples have been presented where the consumption of 2 faradays mol^{-1} was observed for reactions in which electrogenerated radicals abstract hydrogen atoms from DMF.[17] Our finding that 2 faradays of electrons are consumed/mol of ketone reacted are consistent with either pathway A or pathway B where Z• is subsequently reduced.

The results of the electrolysis in DMF-d_7 indicate that 30% of the products result from removal of a deuterium from the solvent. Since both the electrolyte cation, Bu_4N^+, and residual H_2O are likely to be better proton donors than DMF,[22] we believe these results indicate that the labeled product results from deuterium atom abstraction from the solvent. Hydrogen atom abstraction from the electrolyte, Bu_4N^+, must also be considered in light of a recent report that phenyl radicals abstract hydrogen from Bu_4N^+ in dimethyl sulfoxide.[23] Hydrogen atom abstraction by phenyl radicals from Bu_4N^+ is, however, more than 10^2 slower than from DMF when the concentrations of Bu_4N^+ (0.1 M) and DMF (19.2 M) are taken into account.[24] The relative amount of hydrogen atom abstraction from DMF occurring in reactions in protiated DMF is likely to be greater than 30% since a substantial kinetic isotope effect is expected for the hydrogen atom abstraction step.[25] This will allow reduction of the primary alkyl radical to compete more effectively in the case of deuterium atom abstraction.

We are left then with the conclusion that both pathway A and pathway B may operate in this reaction. The coulometric data do, however, indicate that in pathway B the solvent-derived radical (product of step M6) is subsequently reduced, giving an overall stoichiometry of 2 faradays mol^{-1}.

Cyclic Voltammetry of DMP^+-Mediated Reductions of Unsaturated Ketones. The cyclic voltammetric results demonstrate a clear catalysis of the reduction of ketones by DMP^+. The increase in peak current of the DMP^+ cathodic peak in the presence of ketone is due to reaction M2, which regenerates DMP^+ near the electrode surface where it can be reduced again. At higher [ketone], reaction M2 should be faster and the current due to catalysis should increase. The observed behavior is in accord with this qualitative picture.

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(18) Neta, P. *Advances in Physical Organic Chemistry*; Academic: New York, 1976; Vol. 12, pp 253–270.
(19) Beckwith, A. L. J. *Tetrahedron* **1981**, *37*, 3073.
(20) It is worthwhile to note that no pinacol was observed in the reduction of 6-hepten-2-one in the presence of 0.5 M water. This result is in sharp contrast to results in diglyme solvent where reduction in H_2O, 0.3 M diglyme gave the corresponding pinacol in high yield.[1] We have no explanation to offer for the differing results in the two solvents.
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The shape of the cyclic voltammogram of DMP^+ is unusual and exhibits a sharp rise of the current in the cathodic scan. This peak shape is typical of the electrogeneration of solids and is the result of the nucleation and growth processes involved. The kinetics of the nucleation and growth involved in the formation of $(DMP)Hg_5$ have been elucidated.[2] The steep rise in current is associated with the formation of critical nuclei. In other words, reduction proceeds slowly until a viable number of reduced species form critical nuclei, which allow crystallization, whence the rate of crystal growth (and consequently the current) increases dramatically. The steep rise of the cathodic current of DMP^+ is lost in solutions of increasing [ketone]. This seems to be an indication that at potentials positive of the critical potential (at which critical nuclei are formed) small islands of $(DMP)Hg_5$ are formed that are of insufficient size and structure to form critical nuclei but can be effective in transferring electrons to the ketone. Substantial currents could then be observed, positive of the onset of nucleation, and the wave shape for DMP^+ would be altered. A close examination of the shapes of the cathodic waves reveals that they retain a phase in which the current rises steeply even when 6-hepten-2-one is added. That steep increase in current is gradually obscured as the [6-hepten-2-one] is increased but, when detectable, appears at the same potential as for DMP^+ alone. We believe this steep rise is due to the same nucleation and growth processes as in the case of DMP^+ alone.

The curves in Figure 7 demonstrate that the peak current for DMP^+-catalyzed reduction of **1** is nearly independent of $[DMP^+]$ but directly proportional to [**1**] up to 30 mM. Above 30 mM the peak current continues to increase. In fact, at 130 mM 6-hepten-2-one, the peak current is 64 times that for the DMP^+ alone. Catalysis of this magnitude by a species in solution is, to our knowledge, unprecedented. Typical increases in homogeneous redox catalysis range up to a factor of 10 for very reactive systems.[26] Catalysis such as we observe is more typical for surface-bound catalysts.[27]

The peak current vs [6-hepten-2-one] data in Figure 7 begins to deviate downward from linearity at [6-hepten-2-one] >30 mM. We would expect that at high [6-hepten-2-one] the plots of I_{pc} vs [6-hepten-2-one] would level off as the rate of reaction M2 was sufficient to oxidize each $(DMP)Hg_5$ as it was formed. We did observe a decrease in the slope of the plot at high [6-hepten-2-one] but were unable to obtain reproducible cyclic voltammetric data at such high concentrations ([6-hepten-2-one] >130 mM).

The fact that the peak current is nearly independent of $[DMP^+]$ is consistent with the proposal (see below) that the activity of the solid $(DMP)Hg_5$ is constant.

It is clear from Figure 8 that the effectiveness of the catalysis varies dramatically with the structure of the ketone. We can understand this variation using models derived from homogeneous redox catalysis.[26] From this model we know that the catalytic current (the rate) can depend on the rate of electron transfer (M2), which is directly related to the $E°$ for electron transfer (M2) and the rate of the following reaction(s), like M3. Since the structural variations of the ketones **1**, **5**, and **11** are ≥4 bonds away from the carbonyl group, such variations are unlikely to cause a substantial variation in the $E°$ (or rate) of M2. A more likely source of variation in I_{pc}/I_{pc}^0 is that the rate of the following reaction, step M3, varies with the structure of the ketone. The relative rates are 6-hepten-2-one ≈ 6-heptyn-2-one > 7-octen-2-one > 5-phenyl-2-pentanone. This explanation is consistent with our data and appears to us most reasonable.

Since we know of no other kinetic data with respect to the cyclization of a ketyl radical anion, we turn to data for cyclization of alkyl radicals of structure similar to the ketones we studied. Beckwith and co-workers have reported the rates of cyclization at 25 °C of primary aliphatic radicals: 1-hexenyl, $2.3 \times 10^5\ s^{-1}$; 1-hexynyl, $2.8 \times 10^4\ s^{-1}$; 1-heptenyl, $5.4 \times 10^3\ s^{-1}$.[28] Those rates fall in the same order as do the slopes of the lines in Figure 8. The slope for 5-phenyl-2-pentanone (**7**) is more than 1 order of magnitude smaller than those for the other ketones. Although we have no data for the cyclization of a ketyl or an alkyl radical onto an aromatic ring, it would be reasonable to propose that that rate would be substantially less than the rate for addition to an alkene or alkyne. The methyl radical adds to ethylene roughly 10^2 faster than to benzene at 65 °C.[29]

Polarography of Cyclohexanones. The polarographic data clearly provide evidence for the catalysis of the reduction of ketones by DMP^+. Reduction of DMP^+ at −2.70 V initially results in the formation of the composite $(DMP)Hg_5$, which is then, in turn, oxidized by the ketone, regenerating DMP^+ and Hg^0. The DMP^+ and Hg^0 can then be reduced a second time, a scenario consistent with the increase in limiting current for the DMP^+ wave when ketone is added.

Delahay and Stiehl have developed a quantitative treatment for polarographic measurements of electrocatalysis.[30] They derived an equation for the catalytic current, I_c (eq 10, where m = the flow rate of Hg, t = the drop time, and D = the diffusion coefficient of catalyst C), based on the scheme described in eq 11 and 12. The model involves reversible reduction of the catalyst,

$$I_c = 493nD^{1/2}[C](mt)^{2/3}k_f^{1/2}[K]^{1/2} \quad (10)$$

$$C + ne^- \rightleftarrows R \quad (11)$$

$$R + K \xrightarrow{k_f} C + Y \quad (12)$$

C, followed by an irreversible electron transfer from the reduced catalyst (R) to the substrate (K) and regeneration of the catalyst. It is assumed that reaction 12 takes place near the surface of the electrode and follows bimolecular kinetics.

We did not expect the catalysis with DMP^+ to fully agree with eq 10 since all species in the model of Delahay and Stiehl are soluble, while studies in our laboratory have shown that the reduction product of DMP^+ is insoluble.[3] However, this was the only model solved, and although we expected deviations, we decided to test the effects of the substrate and the DMP^+ concentrations on I_c and compare the effects to eq 10.

I_c was found to vary linearly with $[substrate]^{1/2}$, in agreement with the Delahay and Stiehl solution. Variation of $[DMP^+]$ had almost no effect on I_c. An appropriate modification of eq 10 to account for the independence of I_c on $[DMP^+]$ is to replace [C] with a constant. This is quite reasonable, since $(DMP)Hg_5$ is a solid that deposits on the cathode and it, therefore, has constant activity. In a sense the result shows that regardless of $[DMP^+]$ there is always the same activity of $(DMP)Hg_5$ present at the electrode/solution interface. Polarographic catalytic currents, which are independent of the concentration of catalyst, have been observed in reactions involving U(VI) as the catalyst and nitrate as the substrate.[31] In these cases, like in the case of DMP^+, the reduction product of the catalyst is insoluble.

The effect of water upon the reaction is similar for all four cyclohexanones. The catalytic current increased with increasing $[H_2O]$ at low $[H_2O]$, until it reached a maximum beyond which the current was unaffected by $[H_2O]$. One explanation is that the water is involved in the rate-limiting step at low $[H_2O]$ but at high $[H_2O]$ the rate of the reaction involving H_2O becomes rapid and some other process limits the overall rate.

Two reasonable mechanisms for the reaction are given in Scheme II. Since the ketyl radical anion is a weaker base than OH^-, protonation of the radical anion (step M9) is thermodynamically unfavorable and it is reasonable that it could be slow. Since steps M10 or M11 and M12 occur after the rate-limiting

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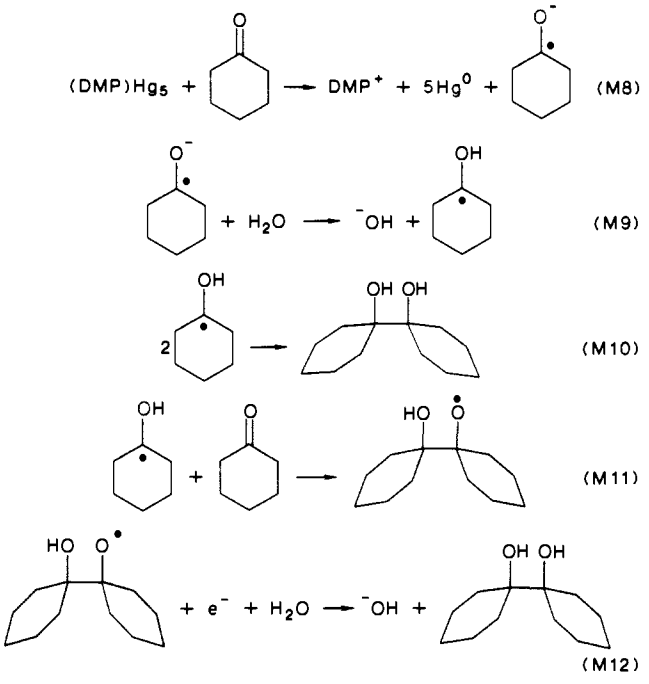
Scheme II



step, kinetic evidence does not allow us to distinguish between those two pathways. We argued that since we observed no effect of $[H_2O]$ on the stereochemistry of the reductive cyclization of 6-hepten-2-one, a step analogous to step M9 was not involved in the mechanism of the reductive cyclization. We believe that this difference results from the differing nature of the fate of the ketyl radical anion in the two reactions. In the case of 6-hepten-2-one, the ketyl can rapidly cyclize. In the case of the cyclohexanones, however, the pathway ultimately leads to dimerization. Dimerization of the ketyl radical anions is expected to be slow since it would involve combination of two anions. Protonation prior to dimerization would allow dimerization to involve radical–radical combination, a reaction expected to be rapid. As we explained earlier, the rate of protonation of the ketyl radical anion (step M9) is expected to be appreciable but is slower than cyclization (step M3). In the case of cyclohexanone reduction, the cyclization pathway is unavailable, and protonation followed by dimerization predominates.

Conclusion

We have presented evidence that dimethylpyrrolidinium ion mediated reductions of ketones at mercury electrodes can lead to the formation of cyclic products. The reaction proceeds with cyclization onto olefinic, acetylenic, or aromatic π bonds and can form 5- or 6-membered rings. The stereoselectivity of the reaction is remarkable, forming nearly exclusively a single isomer in each case. Coulometric and isotope-labeling experiments indicate that the reaction proceeds via attack of the ketyl radical anion on the π bond followed by either hydrogen atom abstraction from DMF or reduction of the resultant radical. Although we have obtained no evidence about electroreductive cyclization reactions at other cathode materials, we believe they are likely to follow a similar path, albeit with a different nature of steps M1 and M2. We believe these DMP^+-mediated reductions to be a general method for the stereoselective synthesis of cyclic alcohols from unsaturated ketones.

DMP^+ mediation directs reduction of ketones toward pathways in which the one-electron intermediates (ketyl radical anions) react in some fashion to form products (either cyclic alcohols or pinacols). Reductions in the absence of DMP^+ (at more negative potentials) typically lead to two-electron processes, reduction of the ketone to the corresponding alcohol.

Redox catalysis studies indicate that DMP^+ is a remarkably effective catalyst for these reductive cyclizations and that the effectiveness of the catalysis depends upon the rate of the cyclization reaction. Polarographic and cyclic voltammetric data are consistent with a mechanism involving initial formation of solid $(DMP)Hg_5$ at the electrode surface. The $(DMP)Hg_5$ in turn transfers an electron to the ketone, regenerating Hg^0 and DMP^+ and forming the ketyl radical anion. The variation of the cathodic peak currents and polarographic limiting currents with [ketone] is similar to that observed in homogeneous redox catalysis of similar systems. The behavior with respect to [catalyst] is markedly different from that observed in homogeneous redox catalysis but can be explained in terms of the reduced catalyst, $(DMP)Hg_5$, being insoluble.

Experimental Section

Electrochemical instrumentation as well as electrochemical procedures were as previously described.[1] Deuteriated dimethylformamide (99% D) was obtained from Aldrich and distilled in vacuo, the middle 60% being retained and stored over activated alumina. DMF was Aldrich Gold Label for preparative experiments and Burdick and Jackson (purified as DMF-d_7) for cyclic voltammetric and mechanistic experiments. 7-Octen-2-one and 5-phenylpentan-2-one were prepared by condensation of the corresponding alkyl bromide with ethyl acetoacetate[32] followed by decarboxylation.[33]

6-Heptyn-2-one was obtained from 3-methyl-2-cyclohexenone by epoxidation followed by treatment with (*p*-tolylsulfonyl)hydrazine.[34]

Preparative electrolyses were carried out to complete consumption of the reactant, typically 2.2 faradays mol^{-1}. Initial currents were 70–90 mA. Purified products were characterized as follows: ^1H and ^{13}C NMR, IBM AC-200 or AC-300; IR, Beckman IR4250; mass spectra, AEI MS-30. Deuterium labeling analysis was conducted on a VG 7070E-HF operating at an ionizing voltage of 20 eV in the selected ion recording mode. Reaction components were separated on a Hewlett-Packard 5890 gas chromatograph equipped with a J&W Scientific 30-m DB-5 capillary column eluting directly into the VG 7070E source.

Gas chromatographic analyses were conducted on a Varian 3740 gas chromatograph equipped with a flame ionization detector. Either a 10 ft × $^1/_8$ in. 10% OV-210, 10 ft × $^1/_8$ in. 10% Carbowax 20 M, 2% KOH, or 20-m Carbowax fused silica column was used. Internal standard techniques were employed.

Medium-pressure chromatography separations used Lobar Lichroprep Si-60 columns, which were eluted with hexane–ethyl acetate mixtures. A Rainin Knauer 188 refractive index detector was employed to monitor compounds eluting from the columns.

Product Identification. Straight-chain alcohols were identified by comparison with compounds prepared from reduction of the appropriate ketone with sodium borohydride.[35]

***cis*-1,2-Dimethylcyclohexanol.** The crude electrolysis product was purified by medium-pressure liquid chromatography, and its spectroscopic data were recorded and found to be identical with data previously reported.[36]

1-Hydroxy-1-methyl-1,2,3,4,6,9-hexahydronaphthalene. The crude product was purified by medium-pressure liquid chromatography. Its melting point, UV spectrum, ^1H NMR, ^{13}C NMR, and mass spectrum were in good agreement with literature data.[6]

1-Methyl-2-methylenecyclopentanol. The crude product was purified by column chromatography on silica gel, eluting with 2:1 hexane–ethyl acetate. Spectral data were found to be identical with literature data.[4]

Acknowledgment. We are grateful to the National Science Foundation for support of this work and to Research Corp. and Grinnell College for partial support of J.E.S. during a leave from Grinnell College. We also thank Dr. Edmund Larka for his assistance in obtaining mass spectral data in order to assay deuterium incorporation in the labeling experiments.

Registry No. 2, 39546-75-3; **5**, 3664-60-6; **7**, 2235-83-8; **8**, 19879-12-0; **10**, 103094-38-8; **11**, 928-39-2; **12**, 61882-70-0; $(DMP)Hg_5$, 104635-03-2; DMP^+, 15312-12-6; $Bu_4N^+BF_4^-$, 429-42-5; Hg, 7439-97-6; *trans*-1,2-dimethylcyclohexanol, 19879-11-9; 5-phenyl-2-pentanol, 2344-71-0; pinacol, 76-09-5; dimethylformamide, 68-12-2.

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