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Communications

Electrochemical Catalysis of a 5-*Endo-Trig* Cyclization in Bicontinuous Microemulsions

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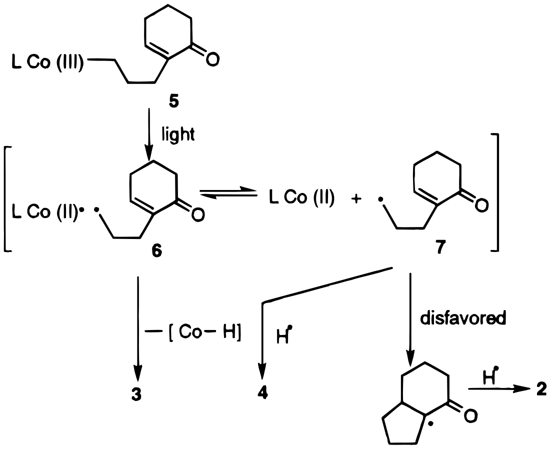
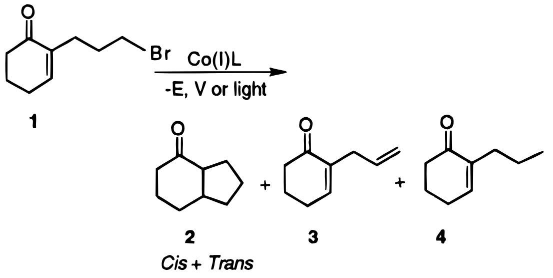
Microemulsions of oil, water, and surfactant are thermodynamically stable, macroscopically homogeneous, low toxicity alternatives to organic solvents.[1] Bicontinuous microemulsions have continuous, dynamic, intertwined oil and water microphases. They easily dissolve ionic catalysts and nonpolar reactants and are particularly useful for electrochemical catalytic synthesis and reaction control.[2,3]

Construction of carbocycles[4] is important in many organic syntheses. We recently used electrochemical catalysis with cobalt complexes[5] in microemulsions to make *trans*-1-decalone in high yields from 2-(4-bromobutyl)-2-cyclohexen-1-one.[3a]

Generally, cyclizations follow Baldwin's rules.[6] A 5-*endo-trig* cyclization is disfavored, requiring severe distortions of bond angles and lengths to achieve the necessary reaction geometry. However, cyclizations can sometimes be directed to a disfavored process. For example, a designed antibody catalyzed an otherwise disfavored 6-*endo-tet* ring closure.[7] In this paper, we report dramatic improvement in the yield of disfavored 5-*endo-trig* cyclization product 4-hydrindanone **2** (eq 1) by using electrochemical catalysis in microemulsions made with cetyltrimethylammonium bromide (CTAB)[8a] or sodium dodecyl sulfate (SDS).[8b]

Scheme 1





(1)

Transformations of 2-(3-bromopropyl)-2-cyclohexen-1-one[9] (**1**) were catalyzed by reducing 0.2 equiv of vitamin B$_{12a}$ (cob(III)alamine, Co(III)L) to Co(I)L in an electrochemical cell with a carbon cloth cathode at 25 °C. Key intermediate **5** (Scheme 1) was obtained by oxidative addition of **1** to Co(I)L, formed electrolytically at -0.9 V versus SCE.[10,11] Upon photocleavage of **5** at this potential, the major product was 2-allyl-2-cyclohexen-1-one (**3**) in both the CTAB microemulsion and DMF (Table 1, entries 1 and 2). The yield of **2** was 20%, in agreement with Baldwin's rules.

The yield of **2** was increased to 62−70% by using electrochemical cleavage at -1.5 V versus SCE in microemulsions (entries 3 and 4) in the dark. Yields of **2** at -1.5 V were again low in DMF, MeOH, and MeOH/water (4:1) (entries 5−7). Catalytic electrolysis of **1** in DMF using vitamin B$_{12a}$ and a Hg cathode[12] at -1.54 V versus SCE gave 2% of **2** and 90% of **4**.

Photocleavage of the cobalt−carbon bond of **5** produces radical **7**$^{5a-c}$ (Scheme 1), which can undergo hydrogen atom abstraction to form **4**,[13] the disfavored ring closure to form **2**, and coupling with Co(II)L and loss of [Co−H][5c] to form **3**.

In electrochemical cleavage at -1.5 V, the reaction proceeds by a different pathway (Scheme 2). Carbanion **8**

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[10] Details of electrolysis are the same as in ref 3a.

[11] For NMR data on **2** and **3**, see the following. (a) ^{1}H NMR of **2**: Miyano, M.; Stealey, M. A. *J. Org. Chem.* **1982**, *47*, 3186−3188. ^{13}C NMR of **2**: Cicero, B. L.; Weisbuch, F.; Dana, G. *J. Org. Chem.* **1981**, *46*, 914−919. (b) ^{1}H and ^{13}C NMR of **3**: Barillier, D.; Benhida, R.; Vazeux, M. *Phosphorus, Sulfur Silicon* **1993**, *78*, 83−95.

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[13] An authentic sample of **4** was prepared according to ref 9, by using 1-propyl bromide.

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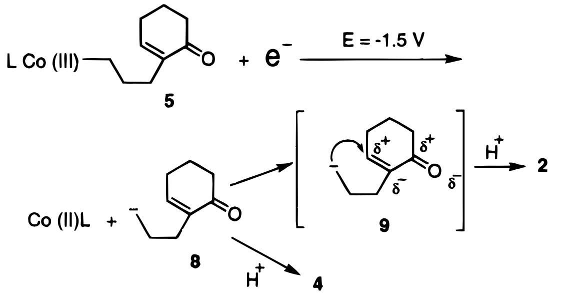
Table 1. Products from Catalytic Electrolyses of 1 Using Vitamin B_{12a}

entry	reaction medium	$-E$, V, vs SCE	time, hour	**2** *cis* + *trans*	yield, %[a] **3**[b]	**4**[b]
1	CTAB μE[c]	0.9 + vis light	4	24	65	3
2	DMF/0.1 M TBAB[d]	0.9 + vis light	4.5	21	51	9
3	CTAB μE[e]	1.5	5	70[f]	0	29
4	SDS μE[g]	1.5	4	62[h]	0	21
5	DMF/0.1 M TBAB	1.5	1.5	19	0	9
6	MeOH/0.1 M TBAB	1.6	1	7	0	50
7	MeOH/water (4/1,v/v)/0.1 M TBAB	1.5	2	10	0	85
8	CTAB/1-pentanol/ water (6%/7%/87%)	1.5	4	46	0	49

[a] Average from GC analysis of three electrolyses, no starting material found in any electrolyses. [b] **3**:**4** ratio estimated by ^{1}H NMR. [c] Microemulsion composition: CTAB/1-pentanol/tetradecane/water = 17.5/35/12.5/35 (wt %). [d] TBAB = tetrabutylammonium bromide. [e] Electrolysis at −1.5 V without vitamin B_{12} recovered 82% of **1** in CTAB microemulsion. [f] *Cis*/*trans* = 4/1. [g] SDS/1-pentanol/tetradecane/water = 13.3/26.6/8/52 (wt %). [h] *Cis*/*trans* = 6.3/1.

Scheme 2



formed by reduction of **5** is a likely intermediate.[5a,b] This is strongly supported by the disappearance of **3**, which cannot form from **8**, in the product mixtures (entries 3−8). Cyclization of **8** is facilitated in the microemulsion to improve the yield of **2**.

Electrolysis at −1.5 V gave low yields of **2** in DMF and MeOH (entries 5 and 6), consistent with Baldwin's rules. Mass recoveries in these electrolyses were also low, suggesting routes to undetectable products.[14] In 4:1 MeOH/water, the yield of **2** remained low, but the yield of **4** increased to 85% (entry 7).

Electrolysis at −1.5 V in a CTAB/pentanol/water solution gave significantly less **2** (46%, entry 8), but nearly twice the amount of **4** compared to the CTAB microemulsion (entry 3). This result suggests that tetradecane is necessary for the best yields of **2**.

These results suggest that the pathway to **2** is faster than formation of **4** in the microemulsions. These fluids have surfactant layers at both oil−water and electrode−microemulsion interfaces.[1] The results also imply that the cyclization of **8** occurs at a site with a low concentration of proton donor, such as one of the interfacial surfactant layers, or in the oil phase. There is considerable precedent for a strong influence of surfactant films on electrodes in electrochemical catalysis. For example, bimolecular rate-determining steps can be enhanced by reactant preconcentration in a surfactant layer on an electrode in a microemulsion.[1a,b,d,2b,c]

In summary, a 5-*endo-trig* cyclization was remarkably facilitated in microemulsions, providing a new example of electrochemical reaction control by these microheterogeneous fluids. The method provides an attractive alternative for the formation of fused five-membered rings under mild conditions.

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Supporting Information Available: Details of experiments and characterization data (3 pages).

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(14) Preliminary spectroscopic analysis of catalyst recovered from DMF after electrolysis suggested the possibility of coupling of intermediates (e.g., **7** or **8**) with vitamin B_{12}.