Novel and Efficient Isomerization of Allylic Alcohols Promoted by a Tetrapropylammonium Perruthenate Catalyst**

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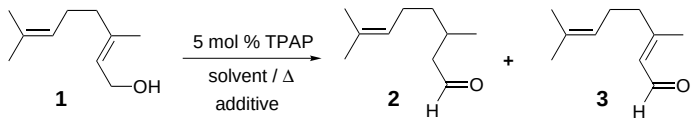
Dedicated to Professor Barry M. Trost

The oxidation of alcohols to aldehydes and ketones is a ubiquitous functional group transformation in organic chemistry.[1] Although stoichiometric amounts of generally noxious reagents are typically employed to effect this conversion, a number of efficient and chemoselective catalytic oxidations of alcohols is slowly emerging.[2] From economic and environmental viewpoints, catalytic processes employing oxygen or H_2O_2 as the ultimate stoichiometric oxidant are the most interesting.[3] In this context, we have recently reported the results of our studies on the ecologically friendly oxidation of alcohols catalyzed either by a copper(I) phenanthroline complex[4] or by tetrapropylammonium perruthenate (TPAP).[5, 6]

During the course of the optimization of the TPAP-catalyzed aerobic oxidation of geraniol (**1**) into geranial (**3**), we sometimes observed the formation of a minor impurity (5–7%) which was identified as citronellal (**2**). Since no citronellol could be detected in the starting material, we concluded that under the aerobic oxidation conditions **1** was somehow transformed into **2**. This intriguing observation prompted us to investigate in greater detail the origin of **2**. Some of our results are collected in Table 1.

Whilst presaturation of the reaction mixture with O_2 (or air) before addition of the ruthenium catalyst completely suppressed the formation of **2** (entry 1), careful degassing led to significantly increased yields of **2** (entry 2). It was also found that running the reaction in the absence of molecular sieves (MS, 4 Å) resulted in improved conversion of **1** into **2**, but did not alter the ratio of **2** versus **3** (entry 3). Furthermore, fluorobenzene proved to be a better solvent than toluene, affording for the first time **2** as the major product (entry 4). To suppress the competitive oxidation of **1** to **3**, we investigated the effect of sacrificial alcohol additives. We were gratified to find that, whilst low molecular weight alcohols led to incomplete transformations and mixtures of **2** and **3** (entries 5 and 6), the addition of a stoichiometric amount of either 1-decanol or 2-undecanol resulted in the quantitative and exclusive formation of **2** (entries 7 and 8).

Table 1. TPAP-catalyzed isomerization of geraniol.



Entry	Solvent	4-Å MS	Additive	Conversion [%][a]	Ratio **2**:**3**[b]
1	$CH_3C_6H_5$	yes	O_2	100	0:100[c]
2	$CH_3C_6H_5$	yes	–	62	47:53[d]
3	$CH_3C_6H_5$	no	–	100	42:58[e]
4	FC_6H_5	no	–	100	72:28[e]
5	FC_6H_5	no	*i*PrOH	72	56:44[e]
6	FC_6H_5	no	2-BuOH	70	73:27[e]
7	FC_6H_5	no	$C_{10}H_{21}OH$	100	100:0[e]
8	FC_6H_5	no	2-undecanol	100	100:0[e]

[a] The conversions were monitored by ^{1}H NMR spectroscopy. [b] The ratios of **2**:**3** were measured by ^{1}H NMR spectroscopy. [c] The reaction mixture was presaturated with O_2 before addition of TPAP. [d] Careful degassing was performed before addition of TPAP. [e] The reaction was effected under argon. Careful degassing is not necessary.

This novel allylic isomerization protocol was then applied to a range of differently substituted allylic alcohols. For practical reasons, 2-undecanol was selected as the preferred sacrificial alcohol. Some pertinent results are displayed in Table 2.

As can be seen from Table 2, monosubstituted (entries 1–3), *cis*-disubstituted (entry 4), *trans*-disubstituted (entries 5–7), and trisubstituted allylic alcohols (entry 8) are all smoothly and quantitatively converted into the corresponding saturated aldehydes and ketones. The reaction is also successful if the C=C bond is enclosed within a ring system (entry 4) or is conjugated with an aromatic substituent (entries 6 and 7).

Although numerous catalysts are known to perform allylic transpositions,[7] they are all restricted to certain substitution patterns in the alkene substrates.[8] To the best of our knowledge, the TPAP/2-undecanol system is the first ruthenium catalyst that tolerates such a broad range of allylic alcohols.

A plausible mechanism that accounts for our current observations is shown in Scheme 1. We believe that the initial steps of the catalytic cycle involve the sequential reduction of the Ru^{VII} complex to a Ru^{III} species. This reduction is accompanied by the concomittant and chemoselective oxidation of two equivalents (per ruthenium) of 2-undecanol (**4**) into the corresponding ketone **5**.[9] The allylic alcohol **6** then interacts with the Ru^{III} catalyst, generating the ruthenium alkoxide **7**.[10] Subsequent β-hydride elimination affords the ketone–ruthenium species **8**, which undergoes a [1,4]-hydride addition to form the ruthenium enolate **9**.[11] At this stage,

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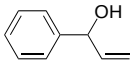
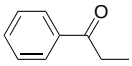
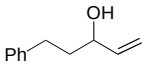
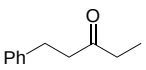
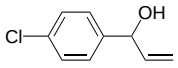
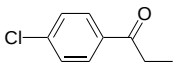
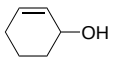
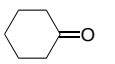
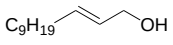
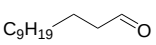
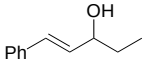
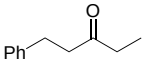
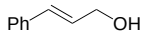
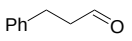
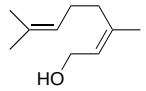
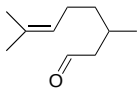
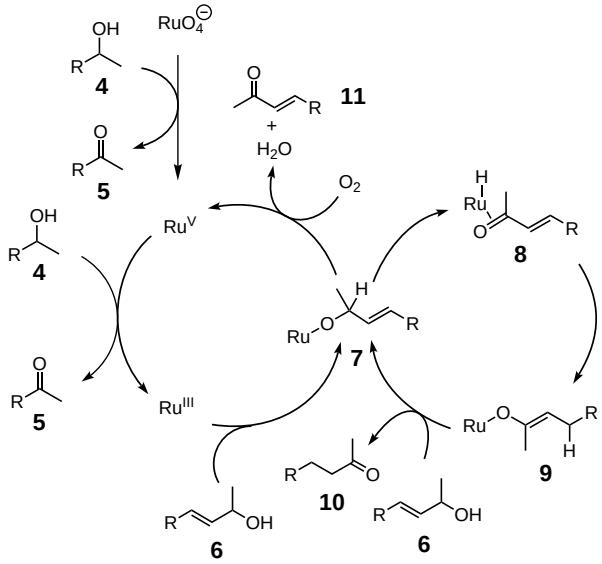
Table 2. TPAP-catalyzed isomerization of allylic alcohols.

Entry	Substrate	Product	Yield [%][a]
1			90
2			92
3			87
4			89
5			41
6			71
7			48
8			52

[a] All yields refer to pure, isolated products. Conversions were quantitative in all cases. The discrepancy between the yields of the isolated products and the conversions reflects the mechanical losses in isolating some of the products.



Scheme 1. Proposed mechanism for the isomerization of allylic alcohols. $R = (CH_2)_8CH_3$.

ligand exchange between enolate **9** and allylic alcohol **6** takes place, releasing ketone **10**[12] and regenerating the ruthenium alkoxide **7**, which reenters a new catalytic cycle. The key roles played by the saturated alcohol additive can now be fully appreciated. Not only does **4** generate the active ruthenium catalyst by double reduction of TPAP, but its faster rate of oxidation suppresses the unwanted oxidation of the allylic alcohol substrate. Unless the isomerization is conducted in a glove box, unavoidable traces of oxygen always permeate the reaction vessel and rapidly oxidize the Ru^{III} alkoxide **7** into the Ru^{V} species with concomittant formation of H_2O and enone **11**. The saturated alcohol **4** then performs another important task. By immediately reducing the ruthenium(v) oxidant into the active Ru^{III} species, **4** restores the allylic isomerization cycle. This mechanistic scheme also unites our previously reported TPAP-catalyzed aerobic oxidation of alcohols with the presently observed allylic shift.[9] Indeed, whilst the isomerization involves a Ru^{III} species, the aerobic oxidation of alcohols takes place through the Ru^{III}/Ru^{V} manifold through rapid reoxidation of the low-valent ruthenium alkoxide catalyst **7** by oxygen.

In summary, we have shown for the first time that TPAP, an excellent oxidant, is transformed in situ into a low-valent species which is able to catalyze efficiently the transformation of allylic alcohols into the corresponding saturated carbonyl derivatives. Further work is now directed towards delineating the scope of this reaction and understanding the intimate mechanistic details of this unique catalytic system.

Experimental Section

Typical procedure for the isomerization of 1-phenylprop-2-enol to propiophenone (Table 2, entry 1): A solution of 1-phenylprop-2-enol (214 mg, 1.6 mmol) and 2-undecanol (252 mg, 1.6 mmol) in fluorobenzene (20 mL) was degassed for 3 min by sonication in an ultrasound bath under a gentle stream of argon. Solid TPAP (34 mg, 0.096 mmols) was then added, and the reaction mixture was heated at reflux under an argon atmosphere. The progress of the reaction was monitored by thin layer chromatography and/or gas chromatography. Upon completion of the isomerization, the reaction mixture was cooled to room temperature and filtered through a celite pad. After the pad was washed with chloroform (30 mL), the combined organic solvents were removed under reduced pressure and the product was purified by column chromatography (silica gel, ethyl acetate:hexane, 1:9). Analytically pure propiophenone was obtained as a colorless liquid (193 mg, 90 %).

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[8] For example, the Trost ruthenium catalyst is ineffective for the isomerization of geraniol (**1**) into citronellal (**2**).[7k]
[9] In general, a greater amount of 2-undecanone (**5**; 30–45%) is produced in these reactions. The difference between the theoretical and the experimental quantities of **5** relates to the reoxidation of the Ru^{III} catalyst into a Ru^{V} species by the adventitious presence of O_2. The subsequent reduction of the Ru^{V} complex back to the active, low-valent Ru^{III} derivative necessarily requires the further consumption of the sacrificial alcohol **4**. See also: S.-I. Murahashi, T. Naota, N. Hirai, *J. Org. Chem.* **1993**, *58*, 7318.
[10] That a ruthenium alkoxide **7** is an intermediate in this process is clearly revealed by the complete lack of reactivity of the trimethylsilyl ether derived from **6**.
[11] The [1,4] addition of ruthenium hydrides to enones is well-documented; see for example: Y. Ishii, K. Osakada, T. Ikariya, M. Saburi, S. Yoshikawa, *J. Org. Chem.* **1986**, *51*, 2034. For a similar mechanism involving the [1,4]-hydride addition to conjugated iminium intermediates, see, for example: S.-I. Inoue, H. Takaya, K. Tani, S. Otsuka, T. Sato, R. Noyori, *J. Am. Chem. Soc.* **1990**, *112*, 4897.
[12] Beside being a by-product of the oxidation of **4**, 2-undecanone also appears to act as a ligand for the low-valent ruthenium catalyst.

Nanospheres from Polymerized Lipofullerenes**

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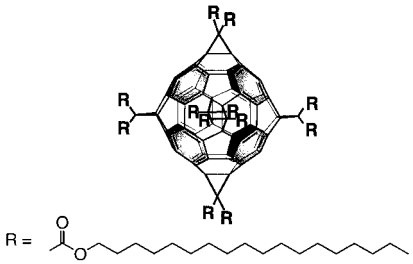
We have shown recently that dipalmitoylphosphatidylcholine (DPPC) self assembles to multilamellar vesicles (MLVs) in an aqueous medium with a high content of lipophilic hexakisadduct of C_{60}, such as **1**, while the incorporated lipofullerene forms rodlike fullerene nanoaggregates within the lecithin bilayers.[1, 2] These intercalated lipofullerene



1

structures are several μm long, have diameters up to 30 nm, and significantly change the micromechanical properties of these composite membrane systems. As an example, an increase of the bending stiffness of the bilayers is observed, and at the same time decoupled lateral diffusion of lipids and lipofullerenes within the double layer has been found.[1–3] In this connection it was of interest as to whether the self assembling of lipofullerenes within these supramolecular structures can be used for the formation of stable nanoarchitectures based on fullerenes.

Herein we report on the synthesis of filled and hollow nanospheres formed upon polymerization of lipofullerenes intercalated into such MLVs. Butadiyne groups have been chosen as polymerizable structural elements within the lipophilic chains. They should allow a covalent linkage between the lipofullerene molecules[7] through a 1,4-addition inside the aggregates upon UV irradiation.[4-6] It is known that membranes built up from lipids with butadiyne units can be polymerized photochemically and give rise to the formation of an oligodiacetylene network.[8] The T_h symmetrical hexakisadduct **2**, which is hyperfunctionalized by its twelve octadecadiynyl side chains, served as the monomeric lipofullerene element. This hyperfunctionality ensures the formation of a perfect network in three dimensions. To synthe-

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