Efficient, Ecologically Benign, Aerobic Oxidation of Alcohols†

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The oxidation of alcohols into aldehydes and ketones can be efficiently performed using catalytic amounts of CuCl·Phen and molecular oxygen or air. This novel, ecologically friendly procedure releases water as the only byproduct.

The transformation of alcohols into aldehydes and ketones is of paramount importance in organic chemistry, both for laboratory-scale experiments and in the manufacturing processes.[1] Unfortunately, the vast majority of the common oxidants have to be used at least in stoichiometric amount. Moreover, they are usually hazardous or toxic and generate large quantities of noxious byproducts.[2] While many ecologically benign processes have been developed for the reduction of carbonyl derivatives,[3] similar procedures have been far less investigated for the oxidation of alcohols.[4]

Despite their obvious economical and ecological importance, few catalytic systems are available for the transformation of alcohols into aldehydes and ketones, using molecular oxygen or air as the ultimate, stoichiometric oxidant.[5] Moreover, most of the currently available catalytic oxidation processes suffer from severe limitations, being usually only effective with reactive alcohols, such as benzylic and allylic ones, or requiring high pressures, temperatures, and catalyst loading.

We have already described in preliminary form the discovery of a novel and ecologically friendly, catalytic aerobic protocol for the efficient oxidation of alcohols **1** into carbonyl derivatives **2** (Figure 1).[6]

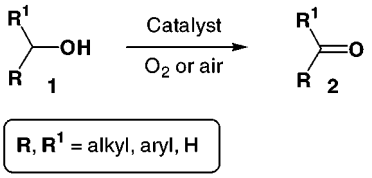

Figure 1.

In this paper, we wish to report full details on the establishment of this useful catalytic process and develop further its synthetic utility. In light of some of our preliminary mechanistic studies, a plausible catalytic cycle will also be discussed.

Our own work in the area of aerobic oxidations was inspired by the exquisite research performed on the structure and reactivity of the binuclear copper proteins,[7] hemocyanin and tyrosinase, and by the seminal contribution of Rivière and Jallabert.[8]

These two authors have shown that the simple copper complex CuCl·Phen (Phen = 1,10-phenanthroline) pro-

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† Dedicated with deep respect to Professor Theodore Cohen.

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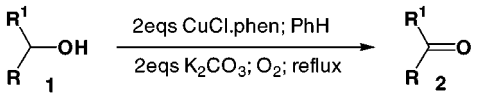


Entry	Substrate	Time	Yield (GC)
1	benzylalcohol	2hrs	86%
2	1-phenylethanol	4hrs	93%
3	4-*t*-butyl cyclohexanol	2hrs	5%
4	3-nonanol	2hrs	18%

Figure 2.

moted the aerobic oxidation of benzylic alcohols to the corresponding aromatic aldehydes and ketones (Figure 2).

Unfortunately, 2 equiv of the copper complex have to be used to achieve good conversions and the system is severely limited to benzylic substrates. Aliphatic alcohols proved to be either unreactive or underwent competing C−C bond cleavage.[9]

Our fascination for the Rivière and Jallabert procedure prompted us to reinvestigate this system and to modify various parameters with the hope of achieving catalyst turnover and establishing a useful and efficient aerobic protocol for the oxidation of all classes of alcohols into carbonyl derivatives.

Our initial experiments were performed on *p*-chlorobenzyl alcohol and employed 2 equiv of CuCl·Phen. It was rather disappointing to find that, besides NaOAc, all the other bases tested were far less efficient than K_2CO_3.[10] However, during the course of these optimization studies, a dramatic influence of the solvent on the reaction rate was uncovered. For example, a 3−4-fold acceleration was obtained when toluene was substituted for benzene. In contrast, replacing benzene by *m*- or *p*-xylene resulted in a decrease in the rate of the reaction. Although it is difficult to offer a rational explanation for the profound effect displayed by minute changes in the structure of the solvent, it is quite reasonable to assume that the coordinating properties of these aromatic solvents may alter significantly the stability and reactivity of the copper complexes.[11] Finally, it was also discovered that molecular oxygen could be replaced by air, a more readily available and inexpensive stoichiometric oxidant.[12]

But the real breakthrough was achieved when it was decided to lower the amount of the catalyst (Figure 3). Under the original Rivière and Jallabert conditions (2 equiv of CuCl·Phen; *benzene*) any attempt at decreasing the concentration of the catalyst resulted in a disastrous curtailment in the reaction conversion. However, *in*

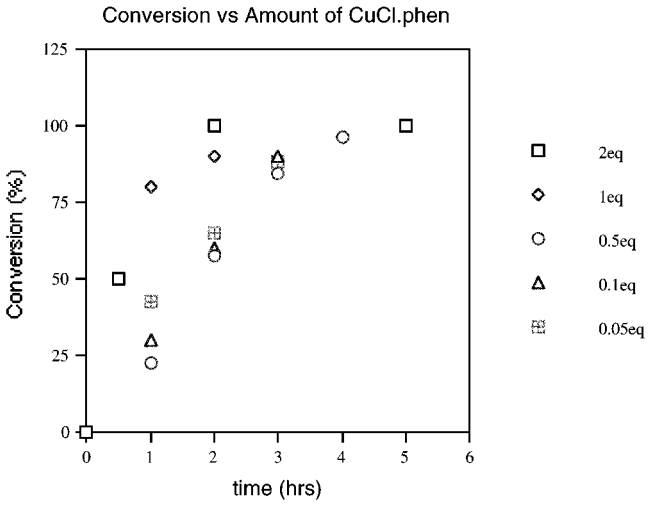


Figure 3.

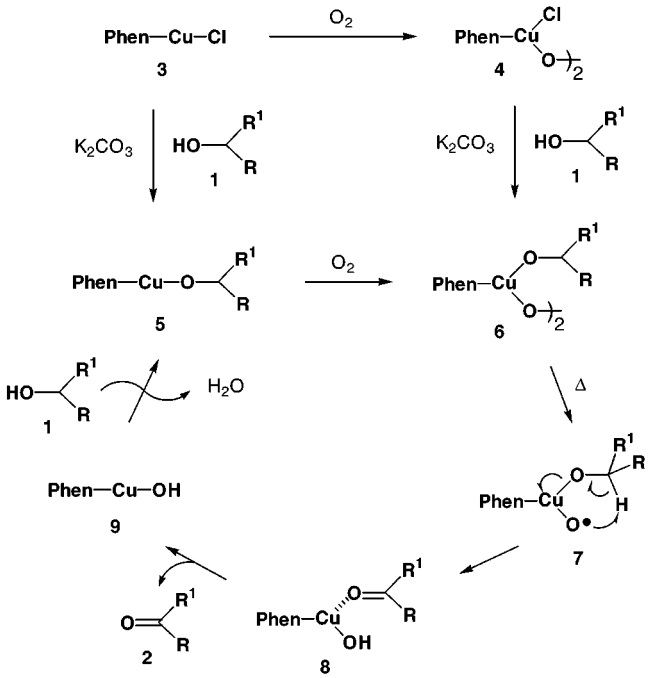


Figure 4.

toluene, reducing the quantity of the copper chloride·Phen complex did not impair the oxidation of the benzylic alcohol. Although the reaction took longer to reach completion, *quantitative formation of p-chlorobenzaldehyde could be accomplished using as little as 0.05 equiv of the catalyst*.

Unfortunately, this initial catalytic system proved, among other things, to be severely restricted to benzylic alcohols. On the basis of previous work in the biochemistry of hemocyanins and tyrosinases,[7] a reasonable mechanism for this aerobic oxidation could be envisioned in which the μ^2-peroxide **6** occupies a cardinal position (Figure 4). This intermediate **6** can be formed by two different pathways: (1) either by the displacement of the chloride ion in complex **3** by the alcohol nucleophile,[13]

(9) See, for example, ref 8a.

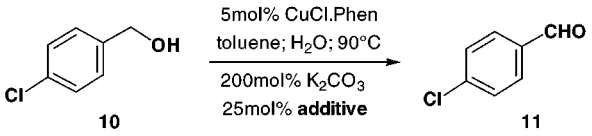
(10) Other bases tested include, e.g., Na_2CO_3, Li_2CO_3, Na_2HPO_4, NaH_2PO_4, Al_2O_3, NaOAc, KOAc, KOH, and $CuCO_3$. Only $KOBu^t$ appears to act as an efficient base in the catalytic oxidation process. Its use is, however, limited at present to the oxidation of secondary alcohols (Markó, I. E.; Gautier, A.; Chellé-Régnaut, I.; Mutokole K. Unpublished results).

(11) Solomon, R. G.; Kochi, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 3300.

(12) The use of air instead of oxygen results in a slower reaction rate. The oxidation can be increased by passing the air through a porous glass frit, which creates microbubbles. Under these conditions, the speed of the catalytic oxidation of alcohols using air matches the one employing oxygen.

(13) The preparation of copper(I) alkoxides and their reactivity toward O_2 has been reported in the literature. See, for example: Capdevielle, P.; Audebert, P.; Maumy, M. *Tetrahedron Lett.* **1984**, *25*, 4397−4400.

Table 1. Effect of the Hydrazine Additives



10 11

entry	additive	conversion (%) 15 min	30 min
1	Me_2NNH_2	10	39
2	$(MeO_2CNH-)_2$	31	56
3	$(EtO_2CNH-)_2$ (DEAD-H_2)	98	>99
4	$(^iPrO_2CNH-)_2$ (DIAD-H^2)	70	99
5	$(MeCONH-)_2$	5	5
6	$(PhCONH-)_2$	<1	<1
7	phthalhydrazide	<1	<1

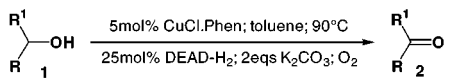
followed by dimerization in the presence of O_2, or (2) by the initial formation of a chloro bis-copper peroxide **4** followed by the exchange of the chloride substituent for the alcohol ligand. The loaded μ^2-peroxide **6** can then undergo homolytic cleavage of the labile O−O bond and generate the reactive species **7**. Intramolecular hydrogen abstraction leads to the copper-bound carbonyl derivative **8** with concomitant reduction of Cu^{II} (or Cu^{III}) to Cu^{I}. Finally, ligand exchange with the starting alcohol and release of H_2O completes the catalytic cycle (Figure 4).

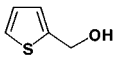
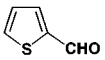
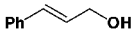
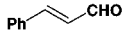
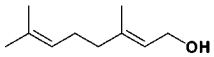
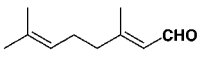
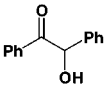
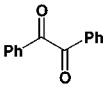
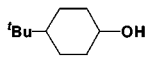
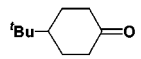
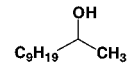
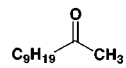
Such a simple mechanistic proposal accommodated the observation that highly activated, benzylic alcohols were good substrates due to the enhanced lability of their α-hydrogen atoms. In contrast, aliphatic alcohols are far less reactive toward H-radical abstraction, and accordingly, poor conversions should ensue. However, it was rather disturbing to note that allylic alcohols, such as geraniol and nerol, displayed poor reactivity in this system.

Furthermore, it was observed that the aerobic oxidation of aliphatic alcohols invariably resulted in the rapid formation of a green copper(II) salt, with concomitant deactivation of the catalyst. This observation strongly suggested that the regeneration of the active copper(I) species was a serious predicament in the oxidation of aliphatic alcohols. It was therefore decided to test the effect of various reductants in this aerobic oxidation reaction. Naturally, we turned to the hydrazine family of reducing agents (Table 1).[14]

Remarkably, addition of hydrazine or *N*,*N*-dimethylhydrazine (20 mol %) to the reaction mixture resulted in a significant enhancement in the rate of the oxidation reaction. The presence of electron-withdrawing groups on the hydrazine led to an even more dramatic improvement both in yield and reaction rate; the oxidation of **10** was virtually complete within 15 min using DEAD-H_2 (Table 1, entry 3). Although the efficiency of the hydrazine additive depended to a small extent on steric hindrance, it was largely affected by electronic factors. For example, while a small methyl ester substituent proved less efficient than the bulkier ethyl group, a more sterically demanding isopropyl ester only reduced slightly the rate of the reaction; complete conversion being observed in 30 min (Table 1, entries 2−4). More importantly, if the ester substituent is replaced by an acyl function, such as acetyl or benzoyl, virtually no oxidation took place, regardless of the s-cis or s-trans conformation of the acyl group (Table 1, entries 5−7). Having found that optimum conversions could be achieved using as little as 25 mol % of DEAD-H_2, we then applied these conditions to the oxidation of a range of representative alcohols. Some pertinent results are collected in Table 2.

Table 2. Copper-Catalyzed Aerobic Oxidation of Alcohols Using DEAD-H_2



Entry	Substrate	Product	Conversion[a]
1			100%
2			100%
3			100%
4			100%
5			80%[b]
6			100%
7			40%[c]
8			44%[d]

[a] The conversions were determined by ^1H NMR spectroscopy and/or by capillary GC analysis. [b] Neral was not detected in this reaction. [c] 20 mol % CuCl·Phen was employed in this reaction.

As can be seen from Table 2, both benzylic and allylic alcohols underwent smooth and quantitative transformation into the corresponding aldehyde or ketone within 1−4 h. It is noteworthy that the catalyst tolerates sulfur heterocycles.[15] The stereochemical integrity of the C−C double bond of the starting allylic alcohols is also retained in the final products, with geraniol giving solely geranial (Table 2, entry 5). Remarkably, trifluoromethyl alcohols and α-ketols are excellent substrates, affording the corresponding trifluoromethyl ketone and α-diketone respectively, in high yield (Table 2, entries 3 and 6).

Interestingly, the corresponding azo dicarboxylate (DEAD) could be substituted to the hydrazide derivative (DEAD-H_2) with equal efficiency.

Unfortunately, both primary and secondary aliphatic alcohols proved to be poor substrates, and only modest conversions could be achieved under these conditions, even when a larger amount of the CuCl·Phen catalyst was employed (Table 2, entries 7 and 8).

A plausible mechanism, involving both the azo and hydrazide derivatives, can be formulated as shown in Figure 5.

(14) Stoichiometric amounts of substituted azo compounds have been used to oxidize magnesium alkoxides to the corresponding carbonyl compounds: Narasaka, K.; Morikawa, A.; Saigo, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2773. The decomposition mechanism of hydrazines in the presence of copper complexes has been reported: (a) Erlenmeyer, H.; Flierl, C.; Sigel, H. *J. Am. Chem. Soc.* **1969**, *91*, 1065. (b) Zhong, Y.; Lim, P. K. *J. Am. Chem. Soc.* **1989**, *111*, 8398.

(15) Alcohols containing nitrogen heterocycles are also smoothly oxidized to the corresponding carbonyl compounds. These heterocycles include pyridine, imidazole, and triazole derivatives.

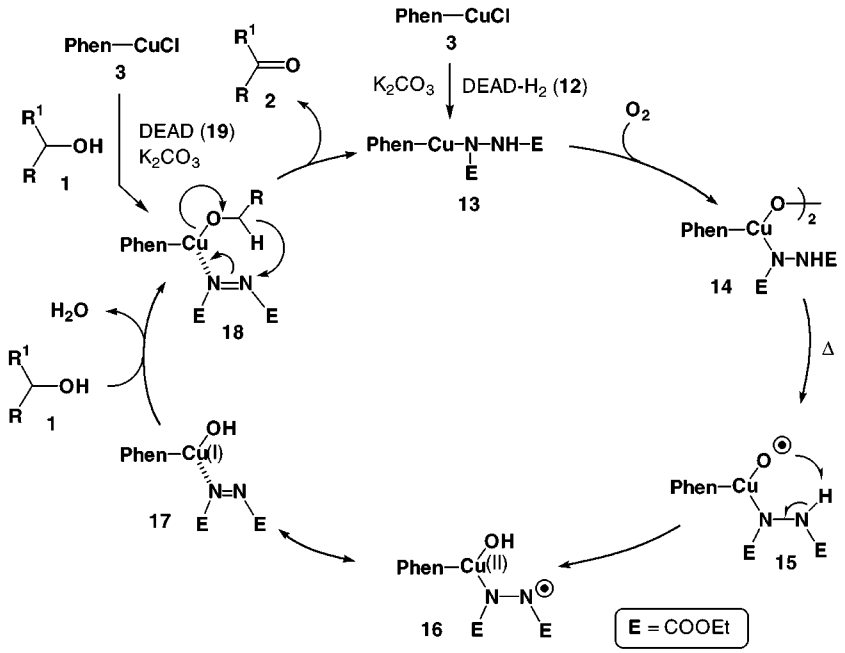


Figure 5.

In the presence of DEAD-H_2 (**12**) and base (K_2CO_3), displacement of the chloride ligand by the hydrazide nucleophile takes place, affording the hydrazino copper-(I) complex **13**.[16] A rapid reaction with oxygen then ensues, leading to the μ^2-peroxo-bis-copper (II) derivative **14**. It is believed that, upon heating, this complex undergoes homolytic cleavage of the labile O−O peroxidic bond resulting in the generation of the copper−alkoxy radical **15**. Intramolecular hydrogen atom abstraction ensues, affording the captodatively stabilized[17] nitrogen-centered radical **16**, which is nothing else than the azo-substituted copper(I) hydroxyl species **17**. This particular sequence is thus responsible for the reduction of the copper(II) species to the catalytically active copper(I) complex. Ligand exchange with the alcohol and concomitant release of H_2O then results in the formation of the ternary loaded catalyst **18**. In this complex, both the alcohol and azosubstituents are held together in close proximity by coordination to the copper center. An intramolecular hydride shift, akin to the Meerwein−Pondorff−Verley−Oppenauer reaction,[18] then takes place, affording transiently a carbonyl-bound hydrazidocopper derivative.[19]

The aldehyde or ketone can now desorb, leading to the initial copper(I) hydrazide complex **13**, which re-enters the catalytic cycle. The replacement of DEAD-H_2 (**12**) by DEAD (**19**) can be easily understood when considering this catalytic cycle. Indeed, several entries to the main catalytic cycle are possible, either via the hydrazino copper species **13** or via the direct formation of the ternary loaded complex **18** from the azo derivative **19**, Phen.CuCl (**3**), and the alcohol **1**. The key role played by the hydrazine or azo compounds can also be readily appreciated when considering this proposed mechanistic rationnale. The hydrazide not only helps in reducing the copper(II) salt to the copper(I) state, but by virtue of its easy passage into the azo derivative, it also acts as a hydride acceptor, allowing the efficient oxidation of the alcohol into the carbonyl compound.

Moreover, we believe that the azo form helps in stabilizing several of the reactive copper complexes involved in this catalytic cycle such as the hydroxycopper complex **17**. Thus, we surmise that this novel catalytic, aerobic oxidation procedure for alcohols into carbonyl derivatives proceeds via a dehydrogenation mechanism and relies on the effective role of hydrazine or azo compounds as hydrogen shuttles and stabilizing ligands for the various copper complexes.[20]

Further evidence for the occurrence of this dehydrogenation mechanism can be gathered from the following experiments. The hydrazidocopper complex **13** can be independently prepared by reacting Phen.CuCl (**3**) with the sodium salt of DEAD-H_2. Addition of an alcohol in the absence of O_2 results in no oxidation to the corresponding carbonyl compound. However, when oxygen is admitted into the reaction medium, rapid and quantitative conversion into the desired product is achieved. Moreover, combining an alcohol with Phen.CuCl and DEAD under anaerobic conditions led to the rapid oxidation of the starting material and the simultaneous generation of equimolar amounts of DEAD-H_2. The

(16) The intermediacy of complex **13** in the aerobic oxidations was supported by the following observations: (1) independently generated complex **13** (CuCl. Phen/DBADH$_2$/NaH) proved to be unreactive under anaerobic conditions; (2) passing O_2 through the reaction mixture containing **13** and alcohol **1** restored the catalytic activity and good yields of aldehyde **2** were again obtained.

(17) (a) Sustmann, R.; Müller, W.; Mignani, S.; Merényi, R.; Janousek, Z.; Viehe, H. G. *New. J. Chem.* **1989**, *13*, 557. (b) De Boeck, B.; Janousek, Z.; Viehe, H. G. *Tetrahedron* **1995**, *51*, 13239−13246

(18) For general reviews on Oppenauer-type oxidations, see: (a) de Graauw, C. F.; Peters, J. A.; Vandekkum, H.; Huskens, J. *Synthesis* **1994**, 1007−1017. (b) Djerassi, C. *Org. React. (N. Y.)* **1951**, *6*, 207−212. (c) Krohn, K.; Knauer, B.; Kupke, J.; Seebach, D.; Beck, A. K.; Hayakawa, M. *Synthesis* **1996**, 1341−1344.

(19) The use of stoichiometric amounts of dipiperidinyl azodicarboxamide to oxidise magnesium alkoxides to the corresponding carbonyl compounds has been described: Narasaka, K.; Morikawa, A.; Saigo, K.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 2773−2776. No reaction is observed under our catalytic anaerobic conditions if DBAD is replaced by the azodicarboxamide derivative.

(20) Another argument against the oxo-transfer mechanism in our catalytic, aerobic, oxidation protocol is the lack of formation of sulfoxides from sulfides, *N*-oxides from amines, and phosphine oxides from phosphines. Alkenes also proved to be inert toward oxidation; no epoxide formation could be detected under our reaction conditions.

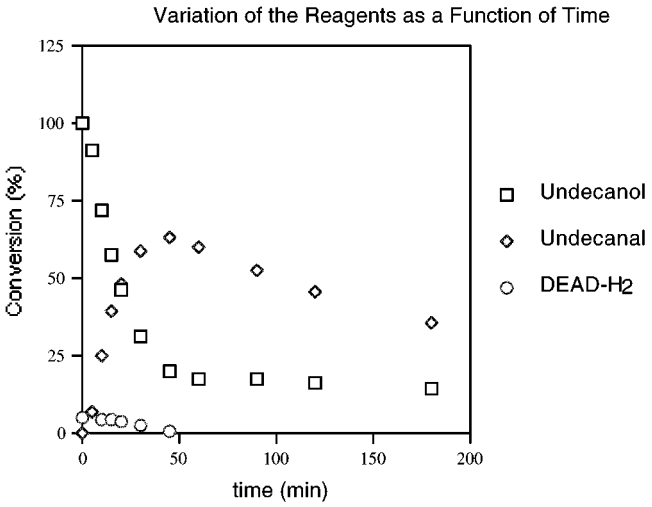


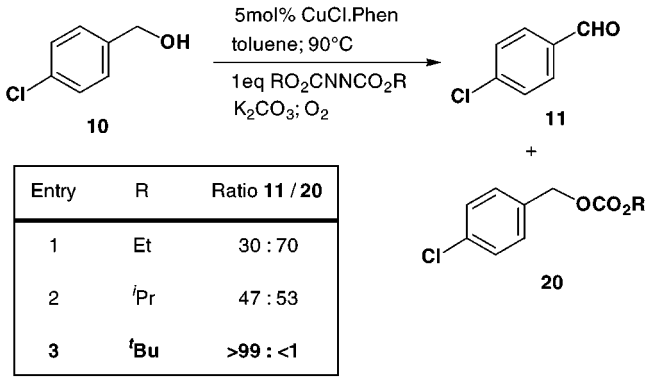
Figure 6.

proportion of aldehyde/ketone and hydrazine formed is equivalent to the quantity of starting azo derivative. Independent reaction of the alcohol with DEAD and K_2CO_3 in the absence of air and copper salts results in the quantitative recovery of the starting alcohol.[21] Although we have not yet been able to obtain direct evidence for some of the intermediates postulated in this catalytic scheme, we believe that the above-mentionned experiments lend credit to the involvement of complexes **13**, **14**, and **18** and strongly support our proposed mechanism.

However, two major observations still need to be accounted for: the lack of reactivity of aliphatic substrates and the need for a 5-fold excess of DEAD or DEAD-H_2 over CuCl·Phen to achieve quantitative oxidations of benzylic and allylic alcohols.

An interesting clue to these questions was provided when the fate of the reagents and products involved in the aerobic catalytic oxidation of undecanol to undecanal was monitored (Figure 6).[22]

Whereas the decay of the alcohol follows the expected kinetic course, the formation of the aldehyde shows an abnormal behavior. In the early part of the reaction, the aldehyde formation matches almost perfectly the disappearance of the alcohol. However, after ca. 50% conversion, it reaches a maximum and then slowly begins to decrease. Clearly, a side reaction is consuming the aldehyde product as soon as its concentration attains a critical value. The fate of the DEAD-H_2 additive is even more interesting. In stark contrast to our expectations, the concentration of DEAD-H_2 does not remain constant throughout the course of the reaction but gradually decreases over time. The disappearance of DEAD-H_2 corresponds exactly to the point of maximum aldehyde formation. Thus, the destiny of the aldehyde and the



Entry	R	Ratio **11** / **20**
1	Et	30 : 70
2	^{i}Pr	47 : 53
3	^{t}**Bu**	**>99 : <1**

Figure 7.

DEAD-H_2 additive are intimately linked, and as the hydrazide is removed from the reaction mixture, the formation of the aldehyde simultaneously stops and its concentration decreases after the hydrazide has been totally consumed. A similar pattern is observed for the related DEAD compound. In this case, however, an initial and extremely rapid transformation of DEAD into DEAD-H_2 takes place. Only the hydrazide can be observed later in the reaction medium. Closer examination of the reaction byproducts using stoichiometric DEAD under anaerobic conditions led to the isolation of unexpectedly large quantity of the mixed carbonate **20** (Figure 7).

Thus, the hydrazide or its azo analogue not only plays a key role in the catalytic cycle as a hydride acceptor and a reductant for the copper catalyst but also acts as an acyl transfer reagent generating competitively the undesired mixed carbonate **20**. This byproduct presumably originates from the inter- or intramolecular nucleophilic attack of the alcohol on either the copper hydrazide or azo complexes **13** or **18**, respectively, resulting ultimately in the deactivation of the catalyst. To minimize this undesired trans-acylation reaction, sterically demanding azo derivatives were tested (Figure 7). While diisopropyl azodicarboxylate (DIAD) produced a more favorable aldehyde/carbonate ratio (Figure 7, entry 2), we were gratified to find that the corresponding di-*tert*-butyl azodicarboxylate (DBAD) led solely to the formation of the desired oxidation product with no trace of the mixed carbonate contaminant (Figure 7, Entry 3).

Under these optimized conditions, the aerobic oxidation of alcohols can be efficiently achieved using as little as 5 mol % of the DBAD or DBAD-H_2 additives (Table 3).

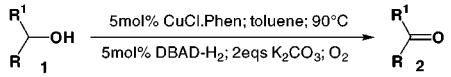
Using this improved and more ecologically friendly protocol, both primary and secondary alcohols are now smoothly oxidized to the corresponding carbonyl derivatives in high yield (Table 3, entries 7−9).

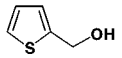
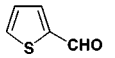
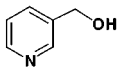
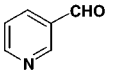
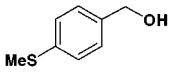
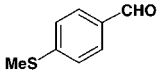
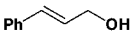
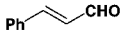
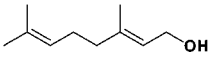
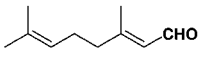
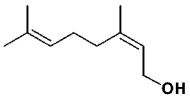
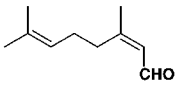
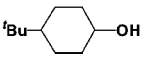
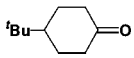
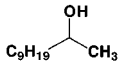
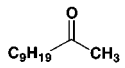
In summary, we have discovered a simple and environmentally friendly, catalytic aerobic protocol for the efficient oxidation of a wide variety of alcohols into aldehydes and ketones. This novel catalytic system uses oxygen or air as the stoichiometric oxidant and releases water as the sole byproduct. Although much remains to be done to understand the intimate mechanistic details of this catalytic oxidation procedure and to further optimize the reaction conditions, we believe that a genuine leap has been realized in the establishment of mild and functionally tolerant, ecologically benign, catalytic systems for the oxidation of alcohols into carbonyl derivatives.

(21) The oxidation of alcohols using azodicarboxylates has been previously reported (Yoneda, F.; Suzuki, K.; Nitta, Y. *J. Org. Chem.* **1967**, *32*, 727−729.). Control experiments were therefore performed to establish the need for copper salts in our oxidation procedure. Thus, under our reaction conditions, no aldehyde or ketone could be detected **in the absence** of the CuCl·Phen catalyst, even if phenanthroline was added as an activating base. Moreover, certain reactive alcohols were oxidized partially by CuCl·Phen **in the absence** of the azo derivative **19**, though only in moderate yields. These control experiments thus clearly establish the key role of the copper ion in these oxidations.

(22) The oxidation reactions were monitored by GC (Permabond SE-52-DF-0.25; 25 m × 0.25 mm i.d.) using tetradecane as the internal standard.

Table 3. Copper-Catalyzed Aerobic Oxidation of Alcohols Using DBAD-H_2



Entry	Substrate	Product	Yield[a]
1			85%
2			81%
3			92%
4			89%
5			71%[b]
6			73%[c]
7			84%[d]
8			88%[e]
9	C_9H_{19}—CH_2OH	C_9H_{19}—CHO	65%

[a] All yields refer to pure, isolated compounds. [b] Neral was not detected in this reaction. [c] Geranial was not detected in this experiment. [d] 10 mol % CuCl·Phen and 10 mol % DBAD were used in this reaction. [e] 5 mol % DBAD was employed instead of DBAD-H_2.

Experimental Section

General Procedure for the Aerobic Oxidation of Alcohols Using $DEADH_2$ (Procedure A). Preparation of 4-Chlorobenzaldehyde. A 25 mL, two-necked flask was fitted with a reflux condenser and an oxygen inlet. Toluene (10 mL) was added followed sequentially by CuCl (9.9 mg; 0.1 mmol; 5 mol %) and phenanthroline (18 mg; 0.1 mmol; 5 mol %). The black complex that formed was stirred at room temperature for 10 min. Diethylhydrazinodicarboxylate ($DEADH_2$; 88 mg; 0.5 mmol; 25 mol %) was added followed by solid K_2CO_3 (552 mg; 4 mmol; 200 mol %) and the stirring continued for another 5 min. 4-Chlorobenzyl alcohol (285 mg; 2 mmol) was added neat, and the solution was heated at 90 °C under a gentle stream of oxygen. The oxidation was followed by removing aliquots and analyzing them by TLC, GC, or ^{1}H NMR spectroscopy. After 30 min, the reaction was found to be complete, the mixture was cooled to room temperature and filtered through a pad of Celigel (50% silica gel mixed with 50% Celite), and the solvent was evaporated in vacuo. The crude product was further purified by chromatography on silica gel using CH_2Cl_2 as the eluant. 4-Chlorobenzaldehyde was obtained as a colorless liquid (278 mg; 99%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 9.98 (1H, s), 7.82 (2H, d, J = 8.4 Hz), 7.5 (2H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 191.3, 141.5, 135.4, 131.5, 130.0; IR (film) 1700 cm^{-1}.

Thiophene-2-carboxaldehyde. The oxidation was performed as described above (procedure A) using 230 mg (2 mmol) of thiophene-2-methanol. The title compound was isolated in 81% yield (183 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 9.9 (1H, s), 7.7 (2H, m), 7.2 (1H, t, J = 3.8 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 182.8, 143.9, 136.1, 135.0, 128.2; IR (film) 1673 cm^{-1}.

Acetophenone. The oxidation was performed as described above (procedure A) using 250 mg (2 mmol) of 1-phenylethanol. The title compound was isolated in 94% yield (226 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 7.94 (2H, d, J = 8 Hz), 7.56 (1H, t, J = 8 Hz), 7.45 (2H, t, J = 8 Hz), 2.6 (3H, s); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 198.7, 137.7, 133.7, 129.2, 128.9, 27.2; IR (film) 1706 cm^{-1}.

1,1,1-Trifluoromethylacetophenone. The oxidation was performed as described above (procedure A) using 352 mg (2 mmol) of 1-phenyl-2,2,2-trifluoroethanol. The title compound was isolated in 91% yield (318 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 8.1 (2H, d, J = 7.5 Hz), 7.7 (1H, t, J = 7.5 Hz), 7.6 (2H, t, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 180.0 (q, J = 35 Hz), 135.4, 130.0, 129.9, 129.0, 116.3 (q, J = 292 Hz); IR (film) 1720 cm^{-1}.

Cinnamaldehyde. The oxidation was performed as described above (procedure A) using 268 mg (2 mmol) of cinnamyl alcohol. The title compound was isolated in 89% yield (236 mg): ^{1}H NMR ($CDCl_3$, 200 MHz) δ_H 9.7 (1H, d, J = 7.7 Hz), 7.5 (5H, m), 6.7 (1H, dd, J_1 = 16 Hz, J_2 =7.7 Hz), 6.6 (1H, dd, J_1 = 16 Hz, J_2 = 7.7 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ_C 193.6, 152.7, 133.9, 131.2, 129.0, 128.5, 128.4; IR (film) 1682 cm^{-1}.

Geranial. The oxidation was performed as described above (procedure A) using 308 mg (2 mmol) of geraniol. The title compound was isolated in 69% yield (211 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 10.0 (1H, d, J = 8.1 Hz), 5.8 (1H, d, J = 8.1 Hz), 5.0 (1H, m), 2.2 (4H, bs), 2.1 (3H, s), 1.7 (3H, s), 1.6 (3H, s); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 191.1, 163.6, 132.8, 127.3, 122.5, 40.5, 25.7, 25.6, 17.6, 17.5; IR (film) 1677 cm^{-1}.

Benzyl. The oxidation was performed as described above (procedure A) using 424 mg (2 mmol) of benzoin. The title compound was isolated in 92% yield (388 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 7.9 (4H, d, J = 7.8 Hz), 7.7 (2H, t, J = 7.3 Hz), 7.5 (4H, t, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 195.2, 135.5, 133.7, 130.5, 129.7; IR (film) 1727 cm^{-1}.

4-*tert*-Butylcyclohexanone. The oxidation was performed as described above (procedure A) using 312 mg (2 mmol) of 4-*tert*-butyl-cyclohexanol. The title compound was isolated in 35% yield (108 mg): ^{1}H NMR ($CDCl_3$, 200 MHz) δ_H 2.4 (4H, m), 2.1 (2H, m), 1.5 (3H, m), 0.9 (9H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ_C 212.3, 46.7, 41.2, 32.4, 27.5, 27.3; IR (film) 1720 cm^{-1}.

2-Undecanone. The oxidation was performed as described above (procedure A) using 344 mg (2 mmol) of 2-undecanol. The title compound was isolated in 39% yield (133 mg): ^{1}H NMR ($CDCl_3$, 200 MHz) δ_H 2.4 (2H, t, J = 7.5 Hz), 2.1 (3H, s), 1.56 (2H, m), 1.3 (12H, m), 0.88 (3H, t, J = 6.8 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ_C 208.9, 43.7, 31.8, 29.7, 29.4, 29.1, 23.8, 22.6, 13.9; IR (film) 1721 cm^{-1}.

Aerobic Oxidation Using Stoichiometric Amounts of Dialkylazodicarboxylates. A 25 mL, two-necked flask is fitted with a reflux condenser and a oxygen inlet. Toluene (10 mL) was added followed sequentially by CuCl (9.9 mg; 0.1 mmol; 5 mol %) and phenanthroline (18 mg; 0.1 mmol; 5 mol %). The black complex that formed was stirred at room temperature for 10 min. The dialkylazodicarboxylate (DEAD, DIAD or DBAD; 2 mmol; 100 mol %) was added followed by solid K_2CO_3 (552 mg; 4 mmol; 200 mol %) and the stirring continued for another 5 min. 4-Chlorobenzyl alcohol (285 mg; 2 mmol) was added neat, and the solution was heated at 90 °C under a gentle stream of oxygen. After 30 min, the reaction was found to be complete, the mixture was cooled to room temperature, filtered through a pad of Celigel (50% silica gel mixed with 50% Celite), and the solvent was evaporated in vacuo. The crude product was further purified by chromatography on silica gel using CH_2Cl_2 as the eluant.

Reaction Using DEAD. 4-Chlorobenzaldehyde was isolated in 30% yield (84 mg) together with 4-chlorobenzylethyl carbonate (300 mg; 70%).

4-Chlorobenzylethyl carbonate: ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 7.3 (4H, bs), 5.1 (2H, s), 4.2 (2H, q, J = 7.5 Hz), 1.35 (3H, t, J = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 154.9, 134.3, 133.9, 129.5, 128.6, 68.3, 64.1, 14.1; IR (film) 1745 cm^{-1}; MS (EI) m/z (relative intensity) 214 (M^+, 75).

Reaction Using DIAD. 4-Chlorobenzaldehyde was isolated in 47% yield (132 mg) together with 4-chlorobenzylisopropyl carbonate (242 mg; 53%).

4-Chlorobenzylisopropyl carbonate: ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 7.3 (4H, bs), 5.1 (2H, s), 4.9 (1H, spt, J = 6.3 Hz), 1.3 (6H, d, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 154.5, 134.3, 133.9, 129.6, 128.7, 72.3, 68.3, 21.7; IR (film) 1748 cm^{-1}; MS (EI) m/z (relative intensity) 228 (M^+, 44).

Reaction with DBAD. 4-Chlorobenzaldehyde was isolated in 99% yield (278 mg).

General procedure for the aerobic oxidation of alcohols using $DBADH_2$ (Procedure B). Preparation of 4-Chlorobenzaldehyde. A 100 mL, two-necked flask was fitted with a reflux condenser and an oxygen inlet. Toluene (40 mL) was added followed sequentially by CuCl (40 mg; 0.4 mmol; 5 mol %) and phenanthroline (72 mg; 0.4 mmol; 5 mol %). The dark complex that formed was stirred at room temperature for 10 min. Di-*tert*-butyllhydrazinodicarboxylate ($DBADH_2$; 93 mg; 0.4 mmol; 5 mol %) was added followed by solid K_2CO_3 (2.208 g; 16 mmol; 200 mol %) and the stirring continued for another 5 min. 4-Chlorobenzyl alcohol (1.14 g; 8 mmol) was added neat, and the solution was heated at 90 °C under a gentle stream of oxygen. The progress of the reaction was monitored by TLC. Upon completion of the reaction, the mixture was cooled to room temperature and filtered through a pad of Celigel (50% silica gel mixed with 50% Celite), and the solvent was evaporated in vacuo. The crude product was further purified by chromatography on silica gel using CH_2Cl_2 as the eluant. 4-Chlorobenzaldehyde was obtained as a colorless liquid (1.12 g; 99%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 9.98 (1H, s), 7.82 (2H, d, J = 8.4 Hz), 7.5 (2H, d, J = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 191.3, 141.5, 135.4, 131.5, 130.0; IR (film) 1700 cm^{-1}. Table 2 summarizes the yields obtained for the various substrates oxidized under these conditions.

Pyridine-3-carboxaldehyde. The oxidation was performed as described above (procedure B) using 872 mg (8 mmol) of pyridine-3-methanol. The title compound was isolated in 81% yield (693 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 10.0 (1H, s), 8.99 (1H, d, J = 2 Hz), 8.75 (1H, dd, J_1 = 1.6 Hz, J_2 = 7.2 Hz), 8.09 (1H, dt, J_1 = 1.7 Hz, J_2 = 12 Hz), 7.4 (1H, dd, J_1 = 7.2 Hz, J_2 = 12 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ_C 190.6, 154.5, 151.8, 135.7, 131.3, 123.9; IR (film) 1717 cm^{-1}.

4-Methylthiobenzaldehyde. The oxidation was performed as described above (procedure B) using 1.23 g (8 mmol) of 4-methylthiobenzyl alcohol. The title compound was isolated in 92% yield (1.12 g): ^{1}H NMR ($CDCl_3$, 200 MHz) δ_H 9.8 (1H, s), 7.64 (2H, d, J = 8.2 Hz), 7.2 (2H, d, J = 8.0 Hz), 2.4 (3H, s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ_C 190.8, 147.6, 132.8, 129.7, 125.0, 14.4; IR (film) 1708 cm^{-1}.

Neral. The oxidation was performed as described above (procedure B) using 1.23 g (8 mmol) of nerol. The title compound was isolated in 73% yield (887 mg): ^{1}H NMR ($CDCl_3$, 300 MHz) δ_H 9.9 (1H, d, J = 8.3 Hz), 5.87 (1H, d, J = 8.2 Hz), 5.12 (1H, t, J = 7.6 Hz), 2.6 (2H, t, J = 8.0 Hz), 2.2 (2H, q, J = 8.0 Hz), 2.0 (3H, s), 1.7 (3H, s), 1.6 (3H, s); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ_C 190.5, 163.5, 133.5, 128.5, 122.2, 32.5, 26.9, 25.5, 17.6, 17.4; IR (film) 1675 cm^{-1}.

Decanal. The oxidation was performed as described above (procedure B) using 1.26 g (8 mmol) of decanol. The title compound was isolated in 65% yield (811 mg): ^{1}H NMR ($CDCl_3$, 200 MHz) δ_H 9.8 (1H, t, J = 1.8 Hz), 2.4 (2H, dt, J_1 = 1.8 Hz, J_2 = 7.2 Hz), 1.6 (2H, t, J = 7.3 Hz), 1.3 (12H, m), 0.88 (3H, t, J = 6.1 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ_C 202.7, 43.8, 31.8, 29.4, 29.3, 29.14, 29.07, 22.6, 22.0, 14.0; IR (film) 1716 cm^{-1}.

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