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TEMPO/HCl/$NaNO_2$ Catalyst: A Transition-Metal-Free Approach to Efficient Aerobic Oxidation of Alcohols to Aldehydes and Ketones Under Mild Conditions

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Abstract: Hydrochloric acid, a very inexpensive and readily available inorganic acid, has been found to cooperate exquisitely with $NaNO_2$/TEMPO in catalyzing the molecular-oxygen-driven oxidation of a broad range of alcohol substrates to the corresponding aldehydes and ketones. This transition-metal-free catalytic oxidative conversion is novel and represents an interesting alternative route to the corresponding carbonyl compounds to the metal-catalyzed aerobic oxidation of alcohols. The reaction is highly selective with respect to the desired product when carried out at room temperature in air at atmospheric pressure. Notably, the use of very inexpensive $NaNO_2$ and HCl in combination with TEMPO for this highly selective aerobic oxidation of alcohols in air at ambient temperature makes the reaction operationally and economically very attractive. The results of mechanistic studies, performed with the aid of electrospray ionization mass spectrometry (ESI-MS), are presented and discussed. TEMPO, TEMPOH, and $TEMPO^+$ were observed in the redox cycle by means of ESI-MS. On the basis of these observations, a mechanism is proposed that may provide an insight into the newly developed aerobic alcohol oxidation.

Keywords: green chemistry · homogeneous catalysis · mechanistic studies · oxidation · TEMPO

The oxidation of alcohols to the corresponding carbonyl compounds represents one of the most important functional group transformations in organic synthesis and a vast number of efficient methods have been developed for this transformation.[1] Traditionally, implementing these methods has required the use of stoichiometric oxidizing reagents (e.g., $KMnO_4$, MnO_2, CrO_3, SeO_2, Br_2, etc.), which are generally hazardous or toxic and generate a large amount of environmental effluents.[2] From an economic and environmental viewpoint, there is an urgent need for inexpensive and intrinsically waste-free oxidants and a recyclable catalyst that may be used to perform these transformations.[3a] Therefore, the pursuit of using molecular oxygen or air as the terminal oxidant has attracted intense research interest, and many highly efficient catalyst systems have been developed for selective aerobic alcohol oxidation using transition metal catalysts[4] (mainly copper,[3] palladium,[5,6] and ruthenium[7]), alone or in combination with stable nitroxyl free radicals (e.g., 2,2,6,6-tetramethyl-piperidyl-1-oxy, TEMPO).[8,9] The introduction of TEMPO as a co-catalyst in the transition-metal-based catalytic systems was effective in improving the reaction selectivity under mild conditions. However, deactivation of the transition metal catalysts in these aerobic oxidation systems has been a recurring problem due to water competing with the substrate and/or intermediate for vacant coordination sites on the active metal catalysts.[10] On the other hand, metal-based aerobic oxidation may leave possibly toxic traces of heavy metals in the products. Therefore, the development of an efficient nonmetallic catalyst for the aerobic oxidation of alcohols under mild conditions has long been desired. In this context, we recently disclosed a process for the highly efficient aerobic oxidation of a wide range of primary and secondary alcohols utilizing a TEMPO-based catalyst system that was free from any transition metal co-catalysts.[11a] Subsequent optimization of our initial catalytic system led to an improved and greener protocol whereby benzylic alcohols and secondary

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aliphatic alcohols in water were selectively oxidized to the corresponding aldehydes or ketones in high yield using 1,3-dibromo-5,5-dimethylhydantoin (DBDMH) or *N*-bromosuccinimide (NBS) in place of bromine.[11b] However, two limitations of the reported metal-free catalysis are that an autoclave is required to achieve the required partial pressure of oxygen and that primary aliphatic alcohols are oxidized with only modest selectivity in favor of the formation of aldehydes.[12] In light of the newly developed nonmetal catalytic aerobic oxidation system for alcohols, in the present work we sought to discover and develop another metal-free catalytic system for the highly selective oxidation of alcohols, especially for primary aliphatic alcohols, using dioxygen as the terminal oxidant. Specifically, we centered our efforts on finding a cheaper, greener, and easily available nonmetal reagent as a co-catalyst that could be used in place of Br_2 or DBDMH. A key criterion was that the catalyst would enable us to carry out the oxidation at ambient temperature in air, thereby dispensing with the need for autoclaves and minimizing the risk of explosions on a preparative scale in industrial organic synthesis.

Herein, we describe preliminary results toward achieving these goals and give a full account of the influence of the new co-catalysts on the course of the reactions. We have also obtained further mechanistic insights into these reactions through the application of ESI-MS techniques, which has revealed specific features of this novel transition-metal-free oxidation process that should facilitate catalyst design and screening efforts.

Results and Discussion

TEMPO/halide/$NaNO_2$-catalyzed aerobic oxidation of benzyl alcohol: Recently, interest in the oxidation of alcohols utilizing a nonmetal-driven approach has been burgeoning. Many efficient transition-metal-free systems have been developed for catalytic alcohol oxidation using TEMPO as the catalyst and a variety of nonmetals as the terminal oxidants. These oxidizing reagents include sodium hypochlorite,[13] sodium chlorite,[14] sodium bromite,[15] *tert*-butyl hypochlorite,[16] *N*-chlorosuccinimide (NCS),[17] [bis-(acetoxy)iodo]benzene (BAIB),[18] *m*-chloroperbenzoic acid (*m*-CPBA),[19] trichloroisocyanuric acid (TCCA),[20] oxone,[21] chlorine,[22] and iodine.[23] However, these oxidation methods suffer from one major disadvantage, namely, they depend on substantial amounts of expensive and/or toxic oxidizing reagents, and hence the concurrent production of undesirable waste by-products is intrinsically unavoidable.[12] Recently, an active area of research has emerged, namely, the use of a nonmetal catalyst and dioxygen as the terminal oxidant for selective oxidation of alcohols, and encouraging progress has been made;[24] some of these advances have emanated from our own laboratories.[11c,d]

Our previous studies demonstrated that the TEMPO/Br_2/$NaNO_2$ oxidation system undergoes a sequential cascade reaction involving triple redox cycles, and indicated that each of the cycles may be adjusted to match the activity of the substrate under acidic conditions.[11] Mechanistic studies have shown that TEMPO is a key oxidizing ingredient for alcohol oxidation, while $NaNO_2$ is the cheapest and most convenient source of NO, a recyclable dioxygen activator, under acidic conditions. On the basis of these findings, we focused our attention on finding surrogates for Br_2. A series of halogen-containing compounds, including Bu_4NBr_3, DBDMH, NBS, TCCA, DCDMH, NCS, I_2, HBr, HCl, and HF, was screened using benzyl alcohol as a typical substrate under the standard mild reaction conditions. As can be seen, a wide range of halogen-containing agents proved to be efficient for converting benzyl alcohol to the desired aldehyde with high selectivity (Table 1, entries 1–11). Upon closer analysis of the results of these reactions, we found that the halogen-containing oxidants, such as DBDMH, NBS, TCCA, and NCS, generally cooperated efficiently with

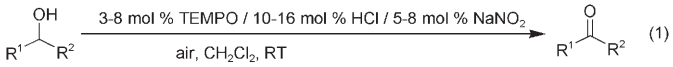
Table 1. Catalytic aerobic oxidation of benzyl alcohol in the presence of TEMPO and catalytic amounts of halides or other surrogates.[a]

Entry	Halide/Acid	*t* [h]	Conv. [%]	Select. [%]
1	Br_2[b]	10	100	100
2	*n*-Bu_4NBr_3[b]	10.5	99.2	100
3	DBDMH[b]	10	55.0	96.7
4	NBS	10	84.9	100
5	TCCA[b]	10	39.0	96.7
6	DCDMH[b,c]	10	44.0	100
7	NCS[d]	10	14.7	86.1
8	I_2[b]	10	34.0	100
9	HBr[e]	10	92.0	98.2
10	HCl[e]	10	100	100
11	HF[f]	10	9.5	48.4
12	HBF_4[g]	10	8.3	65.1
13	HNO_3[g]	10	3.7	100
14	HNO_3[g,h]	10	6.5	81.5
15	HCl[i]	10	3.6	83.3
16	HOAc	10	1.5	66.7
17	TsOH	10	6.5	75.4
18	$MeSO_3H$	10	10.0	67.5
19	CF_3CO_2H	10	7.7	54.5
20	H_3PO_4[j]	10	7.9	59.5
21	H_2SO_4[b,j]	10	21.3	86.4
22	H_2SO_4[b,j]	13[k]	100	100
23	H_2SO_4[b,j]	14[l]	100	100
24	H_3PO_4[b,j]	17[k]	100	100
25	HBF_4[g]	17[k]	100	100
26	$MeSO_3H$	16[k]	100	100
27	CF_3CO_2H	17[k]	100	100

[a] The aerobic oxidation conditions were as follows: benzyl alcohol (5.0 mmol), TEMPO (0.15 mmol), $NaNO_2$ (0.25 mmol), halide (or surrogate) (0.50 mmol), CH_2Cl_2 (8.0 mL), air, ambient temperature. Conversions and selectivities are based on gas chromatography (GC) analyses with area normalization. [b] Halide (or surrogate) (0.25 mmol). [c] DCDMH = 1,3-dichloro-5,5-dimethylhydantoin. [d] NCS = *N*-chlorosuccinimide. [e] HCl = conc. hydrochloric acid, HBr = 40 wt% hydrobromic acid. [f] HF = 40 wt% hydrofluoric acid, reaction in an open anticorrosive plastic tube. [g] HBF_4 = 40 wt% fluoroboric acid, HNO_3 = 65 wt% nitric acid. [h] In the absence of $NaNO_2$. [i] Using the same amount of $NaNO_3$ as a surrogate of $NaNO_2$; the conversion is 59.5% (98.3% selectivity) and 100% (99.5% selectivity) after oxidation for 19 and 25 h, respectively. [j] H_3PO_4 = 85 wt% phosphoric acid, H_2SO_4 = 96 wt% sulfuric acid. [k] In the presence of NaCl (0.50 mmol). [l] In the presence of $BnNMe_3Cl$ (0.50 mmol).

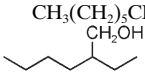
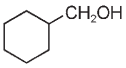
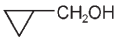
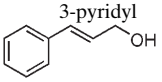
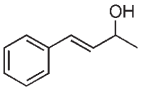
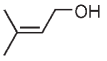
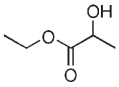
TEMPO and $NaNO_2$ in catalytically oxidizing benzyl alcohol to benzaldehyde. The observations could be rationalized in terms of the positive halogen species being able to oxidize TEMPO/TEMPOH to the oxoammonium cation ($TEMPO^+$). However, we were surprised to find that a few less oxidative halogen-containing compounds, such as HCl and HBr, in combination with TEMPO and $NaNO_2$, were also effective in promoting the catalysis. Of particular interest was the finding that hydrochloric acid, a very inexpensive and readily available inorganic acid, cooperated exquisitely with $NaNO_2$/TEMPO in facilitating aerobic oxidation of the substrate to the corresponding aldehyde under mild conditions (entry 10). In the light of this result, we also screened some other commonly used acids. Unfortunately, the majority of these acids produced only a low conversion of the substrate; only a few acids, for example H_2SO_4, gave a moderate conversion. However, we observed a critical fact from these results, namely that HCl and HBr, two hydrohalogenide acids, yielded extremely high substrate conversions and selectivities. Thus, we presumed that acidic reaction conditions and the existence of chlorine or bromine, whether positive, negative, or neutral, were crucial to obtaining the overall catalytic activity of the TEMPO/$NaNO_2$ catalyst. The role of the acid was assumed to be donation of H^+ to $NaNO_2$ to generate NO/NO_2. The effect of the halide anions on the catalysis may stem from their reaction with NO_2 to generate oxidizing species such as NOX (X = Cl, Br),[25] which are known to oxidize TEMPO/TEMPOH to $TEMPO^+$.[26,27] To verify the importance of the chloride or bromide anions in the catalysis, we carried out the oxidation of benzyl alcohol under standard reaction conditions with a variety of acids in the presence of NaCl or the quaternary ammonium chloride $BnNMe_3Cl$ (Table 1, entries 22–27). The results demonstrated that Cl^- greatly promoted the oxidative conversion of benzyl alcohol to benzaldehyde compared to the reactions without Cl^- (Table 1, entries 18–21). Interestingly, the use of $NaNO_3$ in place of $NaNO_2$ led to a very slow reaction over 10 h, with complete conversion with about 100% selectivity being achieved by prolonging the reaction time to 24 h (entry 15). These preliminary studies revealed that acidic conditions and chloride or bromide anions had beneficial impacts on the catalytic oxidation. Importantly, the results clearly demonstrated that oxidizing positive-halogen-containing compounds were not essential to drive the TEMPO/$NaNO_2$-based catalytic system in the aerobic alcohol oxidation. Being composed of a proton and chloride anion, hydrochloric acid was thus considered to be a promising co-catalyst in combination with TEMPO and $NaNO_2$ for the mild and highly selective oxidation of a broad range of alcohols. During the screening of a variety of reaction conditions, which included varying the amount of catalyst and the solvent used, we found that the catalyst system TEMPO/HCl/$NaNO_2$ could be applied in a wide range of solvents, such as $ClCH_2CH_2Cl$, EtOAc, CH_3CN, HOAc, and PhF, for efficient conversions of benzyl alcohol in air at atmospheric pressure and ambient temperature (without dioxygen or air bubbling).[28]

TEMPO/HCl/$NaNO_2$-catalyzed aerobic oxidation of alcohol substrates: Having established the optimal conditions for the transition-metal-free catalysis, we next examined the range of alcohols to which this catalytic aerobic oxidation [Eq. (1)] could be applied. As revealed in Table 2, all benzylic alcohols were converted into the corresponding benzaldehydes in high isolated yields (entries 1–13). The rates of these benzylic alcohol oxidations were not significantly affected by the electronic properties of the substituents on the benzene ring, an observation that was seemingly at variance with previous studies.[7c,11a,c] Similarly, activated secondary aryl alcohols, such as 1-phenylethanol, 1-phenyl-1-propanol, 1-indanol, and benzhydrol, could be smoothly oxidized to the corresponding acetophenone, propiophenone, 1-indanone, and benzophenone, respectively, in near quantitative isolated yields (entries 15–18). We were pleased to find that primary aliphatic alcohols, which remain difficult recalcitrant substrates in many aerobic oxidation protocols,[4c,11] were oxidized to the expected aldehydes with high conversions and selectivities. For example, complete oxidations of 1-octanol, 2-ethyl hexanol, cyclohexyl carbinol, and cyclopropyl carbinol could be accomplished at ambient temperature and pressure, directly exploiting dioxygen from the air without bubbling (entries 19–22). 2-Phenylethanol could also be oxidized to the corresponding aldehyde with high selectivity (entry 23). Secondary aliphatic alcohols could be completely converted to the corresponding ketones in high isolated yields under the standard mild conditions (entries 24 and 25). In the case of cyclohexanol, slower oxidation requiring 24 h even with method D (entry 26) was observed, possibly as a result of its notable steric effect.[29] The use of HBr in place of HCl led to completion of this reaction with 100% selectivity in 14 h (entry 26). Of particular interest is the fact that 4-(methylthio)benzyl alcohol and 2-thiophene methanol (entries 27 and 28), which are usually regarded as difficult substrates in most aerobic oxidations involving transition metals due to their strong coordinating ability, were also very smoothly converted into the corresponding aldehydes in high yield. In entries 29 and 30, the oxidation reaction was applied to pairs of substrates, both of which bore groups susceptible to oxidation, namely hydroxy and sulfide groups. To our delight, the oxidation system highly selectively oxidized the hydroxy groups to carbonyl groups, whereas the sulfide groups remained intact. Moreover, sulfide groups, which are not compatible with transition-metal-catalyzed oxidation methodology, did not have a deleterious effect on the present oxidation reactions. In the case of 3-pyridylmethanol, slow oxidation was observed and the reaction was incomplete even after 24 h using method C (entry 31). We assume that the HCl was partially neutralized by the basic pyridine. Allylic alcohols such as cinnamyl alco-



(1)

Table 2. Catalytic aerobic oxidations of benzyl and various other alcohols in the presence of TEMPO and a catalytic amount of a halide or other surrogate.[a]

Entry	R^1	R^2	Method	t [h]	Conv. [%]	Select. [%]	Yield [%]
1	Ph	H	A	10	100	100	95
2	2-MeC_6H_4	H	B	10	100	100	97
3	3-MeC_6H_4	H	B	10	100	100	96
4	4-MeC_6H_4	H	B	16	100	100	95
5	2-ClC_6H_4	H	A	13	100	100	96
6	3-ClC_6H_4	H	B	10	99.6	98.0	96
7	4-ClC_6H_4	H	A	15	100	100	96
8	4-FC_6H_4	H	A	10	100	100	95
9	3,5-$F_2C_6H_3$	H	A	10	100	100	97
10	3,5-$(CF_3)_2C_6H_3$	H	A	12	100	100	96
11	4-$MeOC_6H_3$	H	B	15	100	100	98
12	4-$NO_2C_6H_4$	H	B	13	100	100	99
13	4-$MeO_2CC_6H_4$	H	B	12	100	100	97
14	3-$PhOC_6H_4$	H	B	11	100	100	99
15	Ph	Me	B	12	100	100	98
16	Ph	Et	B	12	100	100	98
17			B	16	100	100	98
18	Ph	Ph	B	16	100	100	99
19	$CH_3(CH_2)_5CH_2$	H	D	12	100	94.8[b]	92
20			D	16	100	100	94
21			D	16	98.2	98.6	93
22			C	15	100	100	81
23	$PhCH_2$	H	C	15	73.1	100	–
24	$CH_3(CH_2)_4CH_2$	Me	C	17	100	98.2	96
25	$CH_3(CH_2)_3CH_2$	Et	C	27	98.4	98.5	94
26			D	24	37.3	90.6	–
			D	14	100	100[c]	95
27	4-$MeSC_6H_4$	H	B	11	100	100	99
28	2-thienyl	H	B	12	100	97.0[d]	97
29	$PhCH_2OH$ + PhSMe	B	12	100	100[e]	–	
30	$PhCH_2OH$ + Et_2S	B	14	100	97.9[f]	–	
31	3-pyridyl	H	C[g]	24	92.4	96.6	96[h]
32			C	12	100	100	98
33			D	16	100	98.6	99
34			D	32	100	96.1[i]	84
35			D	31	100	100	89
36			D	29	41.2	100	–

[a] The aerobic oxidation conditions were as follows: alcohol (5.0 mmol), CH_2Cl_2 (8.0 mL), air, ambient temperature. Method A: TEMPO (0.15 mmol), $NaNO_2$ (0.25 mmol), HCl (0.50 mmol); Method B: TEMPO (0.25 mmol), $NaNO_2$ (0.25 mmol), HCl (0.50 mmol); Method C: TEMPO (0.25 mmol), $NaNO_2$ (0.40 mmol), HCl (0.80 mmol); Method D: TEMPO (0.40 mmol), $NaNO_2$ (0.40 mmol), HCl (0.80 mmol); conversions and selectivities are based on gas chromatography (GC) analyses with area normalization. All yields refer to pure, isolated products. [b] Acid (5.2%) was formed. [c] HBr (16 mol%) was used in place of HCl. [d] Approximately 3.0% of 2-chloromethylthiophene was formed. [e] PhSMe remains intact after the reaction. [f] Et_2S remains intact after the reaction. [g] In the presence of 1.2 equivalents of HOAc. [h] A mixture of 3-pyridinecarboxaldehyde and 3-pyridylmethanol was obtained. [i] Approximately 3.9% of 3,3-dimethyl allyl chloride was formed.

hol, (*E*)-4-phenyl-3-buten-2-ol, and 3-methyl-2-buten-1-ol were all completely oxidized with high selectivity (entries 32–34). In addition, some important fine chemicals, such as 3-phenoxy-benzyl alcohol (entry 14), 3-methoxy-2-propyl alcohol (entry 35), and ethyl lactate (entry 36), were efficiently oxidized to the corresponding carbonyl compounds.

Mechanistic studies based on ESI-MS measurements: Recently, ESI-MS[30] has been used as an effective means of resolving mechanistic issues in chemistry and biochemistry.[31] Three reports have dealt with mass spectrometric measurements of the *N*-oxyl radical TEMPO.[32] In these, it was concluded that with normal ESI the radical can be measured both as the molecular ion generated in the electrospray ion source and as the normal protonated molecule. Furthermore, Vainiotalo investigated the mechanism of TEMPO-mediated laccase-catalyzed aerobic oxidation of substituted benzyl alcohols by an ESI-MS method.[32c] To understand the present novel aerobic oxidation reaction, we investigated the reaction mechanism with the aid of ESI-MS. The data shown in Figure 1 provided several useful insights into this aerobic alcohol oxidation catalyzed by a unique combination of TEMPO, $NaNO_2$, and HCl. The interesting findings can be summarized as follows: 1) The $TEMPO^+$ cation seems certain to be involved in the oxidation reactions and to serve as the active oxidant in oxidizing the alcohol substrates. This was indicated by the presence of a signal at m/z 156, corresponding to the $TEMPO^+$ cation, at all times during the reaction processes (see Figure 1d and Figure S2 in the Supporting Infor-

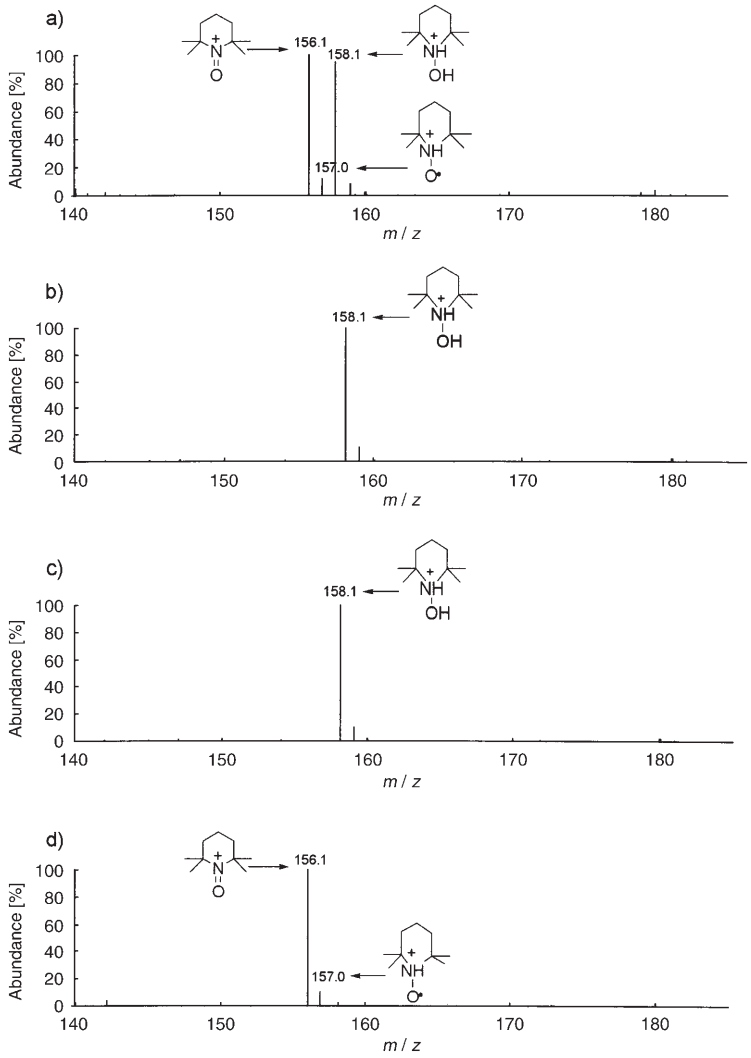


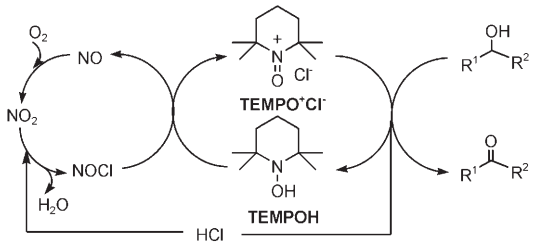
Figure 1. ESI(+) mass spectra obtained under standard conditions from samples taken from a reaction mixture of TEMPO (0.06 mmol) and HCl (0.20 mmol) in MeCN (5 mL) stirred at room temperature in air: a) 10 min after the addition of benzyl alcohol (2.0 mmol), b) after a further 20 min, c) 20 min after the subsequent addition of $NaNO_2$ (0.10 mmol), and d) 3 h after this addition of $NaNO_2$.

mation). 2) Re-oxidation of TEMPOH could be realized, presumably via NOCl. The reduction of NOCl with TEMPOH generated NO. The oxidation of NO by dioxygen in the presence of HCl regenerated NOCl. By comparison with the ESI mass spectrum of a solution of TEMPO in acetonitrile (see Figure S1 in the Supporting Information), we observed some interesting results. For example, when 3 mol% TEMPO was reacted with 10 mol% HCl, we detected new peaks corresponding to $TEMPO^+$ (signal at *m*/*z* 156) and TEMPOH (signal at *m*/*z* 158) (Figure 1a). These results were consistent with those reported in previous studies.[8b] Addition of 100 mol% BnOH to the above reaction mixture led to disappearance of the signal at *m*/*z* 156 with the concurrent formation of about 1.5 mol% benzaldehyde, yet the signal at *m*/*z* 158 remained. This demonstrated that $TEMPO^+$ oxidized the alcohol substrate, while itself being reduced to the corresponding hydroxylamine, TEMPOH. The signal at *m*/*z* 156 could be detected once more following the further addition of 5 mol% $NaNO_2$ to the reaction mixture, an observation that we attribute to re-oxidation of TEMPOH by $NaNO_2$/HCl/O_2. The proposed overall reaction mechanism is presented in Scheme 1.

This mechanism shares similarities with those postulated in our previous studies on transition-metal-free catalyzed oxidations[11a,b] accomplished with some newly-published TEMPO-based systems.[11c,d] The intermediate species observed by ESI-MS, namely $TEMPO^+$ and TEMPOH, may help to confirm the identity of the active species postulated in former publications.[11,24a]

Conclusion

In conclusion, we have shown that the catalyst system HCl/$NaNO_2$/TEMPO permits the selective aerobic oxidation of a broad range of primary and secondary alcohols, which may contain carbon-carbon double bonds or N or S heteroatoms, in air at room temperature. To the best of our knowledge, this is the simplest and the most convenient method among the



Scheme 1. Proposed mechanism for TEMPO/HCl/$NaNO_2$-catalyzed aerobic oxidation of alcohols.

TEMPO-based aerobic alcohol oxidation protocols. It is important to note that the ESI-MS experiments confirmed the existence of $TEMPO^+$ and TEMPOH species, thus providing an insight into the catalytic system. Mechanistically, the $TEMPO^+$ cation has been proved to be central to the cata-

lytic system, and the novel use of NOCl to oxidize TEMPOH plays a crucial role in the TEMPO/HCl/$NaNO_2$ catalytic oxidation cycle. Further investigations will be focused on improving the catalytic activity of the HCl/$NaNO_2$/TEMPO system in order to lower the amount of catalyst required and to shorten the reaction times.

Experimental Section

General conditions: All chemicals were reagent grade and were used as supplied except where noted. All reactions were performed in air at ambient temperature unless specified otherwise. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX-400 instrument and were referenced to Me_4Si ($\delta = 0$ ppm) and residual $CHCl_3$ ($\delta(^1H) = 7.26$ ppm) or $CDCl_3$ ($\delta(^{13}C) = 77.0$ ppm). GC analyses for determining the conversions and selectivities of the reactions were performed on an Agilent 6890N GC system. ESI mass spectra were recorded on an Agilent 1100 Series MSD Trap XCT operated in positive mode. A few representative examples are listed here. Experimental procedures and spectroscopic data for all isolated compounds can be found in the Supporting Information.

General procedure for the TEMPO-catalyzed aerobic oxidation of alcohols: The oxidation of alcohols was carried out in air at ambient temperature in a 50 mL long-necked, round-bottomed flask equipped with a magnetic stirrer. Typically, the alcohol (5.0 mmol) and TEMPO (0.15 mmol) were dissolved in dichloromethane (8 mL). Concentrated hydrochloric acid (0.50 mmol) was added, followed by $NaNO_2$ (0.25 mmol). The resulting mixture was stirred at room temperature and atmospheric pressure. The conversion and selectivity of the reaction were monitored directly by GC analyses without any prior work-up. When GC showed the reaction to be complete, the liquid in the flask was transferred to a separatory funnel. The organic phase was washed with 30 wt% aqueous $Na_2S_2O_3$ solution and saturated aqueous $NaHCO_3$ solution to remove the residual oxidant and TEMPO. The organic layer was dried over anhydrous Na_2SO_4 and concentrated to afford the desired product. Because the selectivities in most reactions were more than 99%, the ^1H and ^{13}C NMR spectra could be recorded directly from the products isolated in this way.

Benzaldehyde: ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 7.47$ (t, 2H), 7.57 (t, 1H), 7.83 (m, $J = 7.2$ Hz, 2H), 9.96 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 125.6$, 126.2, 131.0, 132.9, 188.9 ppm.

3-Methoxyacetone: ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 2.14$ (s, 3H), 3.42 (s, 3H), 4.04 ppm (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 25.8$, 58.8, 77.5, 126.8, 206.2 ppm.

ESI-MS detection: With standard MS detection, we set out to identify any possible intermediates in the reaction process by gradual addition of the reactants. A solution of TEMPO (0.06 mmol) and HCl (0.20 mmol) in MeCN (5 mL) was stirred at room temperature in air. After 10 min, 3 μL of the solution was withdrawn, diluted with 1000 μL of MeCN, and transferred into the ESI source by means of a syringe pump at a flow rate of 5 μL min^{-1} for MS detection (Figure 1a). Benzyl alcohol (2.0 mmol) was then added to the reaction mixture, and after 30 min a further sample was taken and analyzed in the same way, whereupon fewer signals were detected (Figure 1b). Subsequently, $NaNO_2$ (0.1 mmol) was added, and further samples were taken after reaction times of 20 min, 3 h, 6 h, 12 h, and 24 h; MS analyses showed the disappearance of peak at m/z 158 with a re-emergence of the peak at m/z 156, as shown in Figure 1c and d, and Figure S2 in the Supporting Information.

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