Selective Oxidation of Alcohols to Carbonyl Compounds Mediated by Fluorous-Tagged TEMPO Radicals

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Received: November 9, 2004; Accepted: February 4, 2005

Dedicated to Professor Fernando Montanari on the occasion of his 80th birthday

Abstract: Oxidation of primary, benzylic and secondary alcohols into their corresponding aldehydes and ketones with safe, inexpensive oxidants was achieved in good yields under mild conditions in the presence of catalytic amounts of 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) radicals bearing perfluoroalkyl substituents. These "fluorous-tagged" TEMPOs were readily isolated from the reaction products by liquid-liquid or solid-phase extraction, considerably simplifying the purification step. Their recyclability was strongly influenced by the nature of the oxidizing system. The best results were obtained using either [bis(acetoxy)iodo]benzene (BAIB) or aqueous NaOCl as the primary oxidants. Fluorous TEMPO **10** could be reused up to six times in the BAIB oxidation of 1-octanol with only minor loss of catalytic activity.

Keywords: alcohols; aldehydes; ketones; oxidation; TEMPO

Introduction

The selective oxidation of primary and secondary alcohols into the corresponding carbonyl compounds is one of the most important processes in organic synthesis both at a laboratory and industrial scale.[1] Well-established methods for this functional group transformation involve the use of stoichiometric amounts of either inorganic oxidants [e.g., chromium(VI) salts][2] or organic oxidants (e.g., activated DMSO).[3] However, these methods hardly satisfy the current demand for non-polluting chemical processes of high atom efficiency, and new selective procedures which do not generate large amounts of by-products are highly desirable.[4,5] This trend is illustrated by the ongoing development of catalytic systems based on stable nitroxyl radicals such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) in combination with safe and easy to handle primary oxidants.[6,7,8] Early examples of TEMPO-catalyzed reactions included the oxidation of secondary alcohols to ketones with *m*-chloroperbenzoic acid,[9] the oxidation of primary, secondary and benzylic alcohols in an electrochemical process,[10] and the oxidation of allylic and benzylic alcohols to aldehydes by oxygen/CuCl in DMF.[11] In 1987 Montanari and co-workers introduced a far more versatile and efficient catalytic procedure in which buffered bleach acts as the terminal oxidant and bromide ion as a co-catalyst.[12] The oxidation reaction proceeds under mild conditions and both primary and secondary alcohols are converted to carbonyl compounds in high yields, even in large-scale operations. In addition, the oxidation of primary alcohols can be driven to give carboxylic acids by adding a phase-transfer catalyst to the biphasic aqueous/organic system.[13] Inspired by Montanari's work, various research groups have then explored the use of a wealth of other organic and inorganic terminal oxidants {e.g., [bis(acetoxy)iodo]benzene (BAIB),[14] trichloroisocyanuric acid (TCCA),[15] Oxone,[16] or iodine [17]} and anhydrous reaction conditions with the aim of further expanding the already wide applicability of the original procedure.[7] A different approach, pioneered by Semmelhack and co-workers,[11] consists of the use of oxygen as the primary oxidant in conjunction with a TEMPO/metal catalyst combination.[4] The obvious economic and environmental advantages associated with the use of oxygen account for the increasing interest in such catalytic systems.[18,19]

Whichever oxidant is used, separation of TEMPO from the products remains an issue. Moreover, TEMPO is quite expensive, so it is desirable to be able to separate the catalyst after the oxidation reaction and to reuse it. To this end, TEMPO has been immobilized onto both inorganic and organic polymers,[20] affording heterogeneous catalysts, which are readily separated from the reaction mixtures, but are usually far less versatile than the homogeneous TEMPO.[21] A recently emerged option is the immobilization of TEMPO onto soluble polymers, which makes it possible to run the oxidation reaction un-

 DOI: 10.1002/adsc.200404343

der homogeneous or liquid-liquid biphasic conditions. Precipitation of the catalyst is then induced by dilution of the reaction mixture with an incompatible solvent. Soluble polymer-supported TEMPO radicals have been prepared by ring-opening methathesis of norbornene derivatives.[22] Preliminary tests revealed that the activity of these catalysts was consistently lower than that of TEMPO in the oxidation of alcohols under Montanari's conditions. Promising results have been obtained in the oxidation of alcohols with various primary oxidants (including bleach) catalyzed by a TEMPO derivative tethered onto commercially available poly(ethylene glycol) (PEG) of molecular weight of about 5000 Da.[23] The catalyst was easily recovered by selective precipitation from Et_2O and its recyclability was studied using the oxidation of 1-octanol with the mild oxidant BAIB as a model reaction. An independent study on the catalytic performance and recyclability of a series of PEG-supported TEMPO derivatives in the oxidation of alcohols under Montanari's conditions has been recently disclosed.[24] Low molecular weight PEG supports afforded highly active catalytic systems, but poor recovery yields by precipitation with Et_2O. On the other hand, TEMPO tethered onto PEGs with a molecular weight >5000 Da were efficiently recovered, but a pronounced reduction in catalytic activity was observed, especially upon recycling. It appears that coiling of the PEG polymeric backbone around the TEMPO moiety might prevent the access of the substrate to the active site of the catalyst.

Recyclable TEMPO catalysts can be designed without recourse to polymeric supports with all their drawbacks. Indeed, we recently developed a TEMPO derivative bearing perfluoroalkyl substituents (a "fluorous-tagged" TEMPO) which is a selective catalyst for the oxidation of alcohols under mild, homogeneous conditions.[25] The peculiar solubility properties ensured by the presence of the highly fluorinated domain allowed the easy recovery of the catalyst by liquid-liquid extraction of the reaction mixture. In this paper the preparation of a series of fluorous-tagged TEMPO radicals and their activity as catalysts in the oxidation of alcohols are fully accounted. The influence of the linkage between the TEMPO moiety and the fluorous domain on the selectivity of the catalytic system, the use of various primary oxidants and the recoverability of the different catalysts are also discussed.

Results and Discussion

Synthesis of Fluorous-Tagged TEMPO Radicals

The simplest TEMPO derivatives **1–4** (Figure 1) bearing just one fluorous ponytail and having a similar weight percentage of fluorine (about 50%) were readily synthesized following standard procedures. Compound **1** was prepared from the commercially available precursors 4-hydroxy-2,2,6,6-tetramethylpiperidine-1-oxyl radical (**5**; 4-hydroxy-TEMPO) and pentadecafluorooctanoyl chloride (**6**) as described in the literature.[26] Radical **2** was obtained in 40% yield *via* esterification of **5** with 3-(*n*-perfluorooctyl)propionyl chloride (**7**)[27] in dry Et_2O in the presence of Et_3N. The fluorous radicals **3** and **4** were analogously prepared in 28% and 30% yields, respectively, from 4-amino-2,2,6,6-tetramethylpiperidine-1-oxyl (**8**; 4-amino-TEMPO) and the corresponding fluorous acyl chlorides.

As expected, the light fluorous TEMPO derivatives **1–4** are freely soluble in conventional organic solvents, such as CH_2Cl_2 and MeOH, and their partition coefficients P in perfluorocarbon/organic solvent biphasic mixtures are <1 ($P=[\text{Radical}]_{\text{Perfluorocarbon}}/[\text{Radical}]_{\text{Organic Solvent}}$). As a higher fluorine content and an increased number of perfluoroalkyl substituents R_F

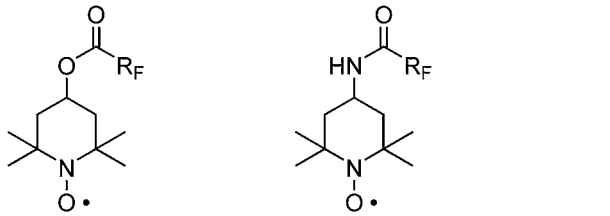
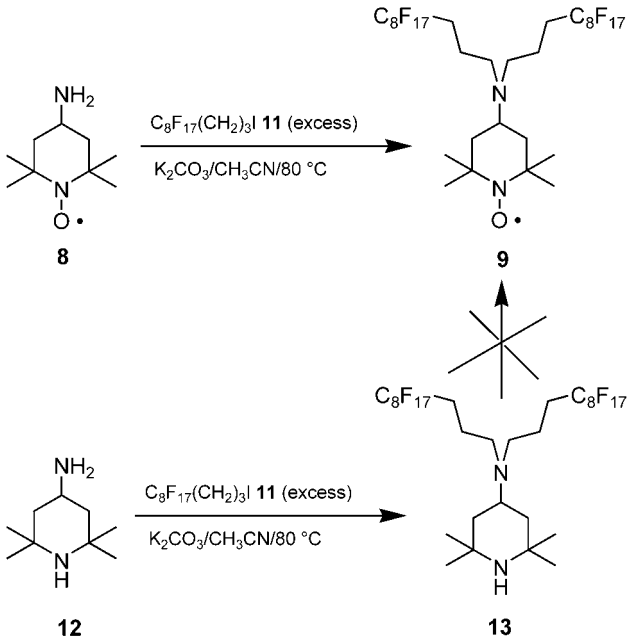
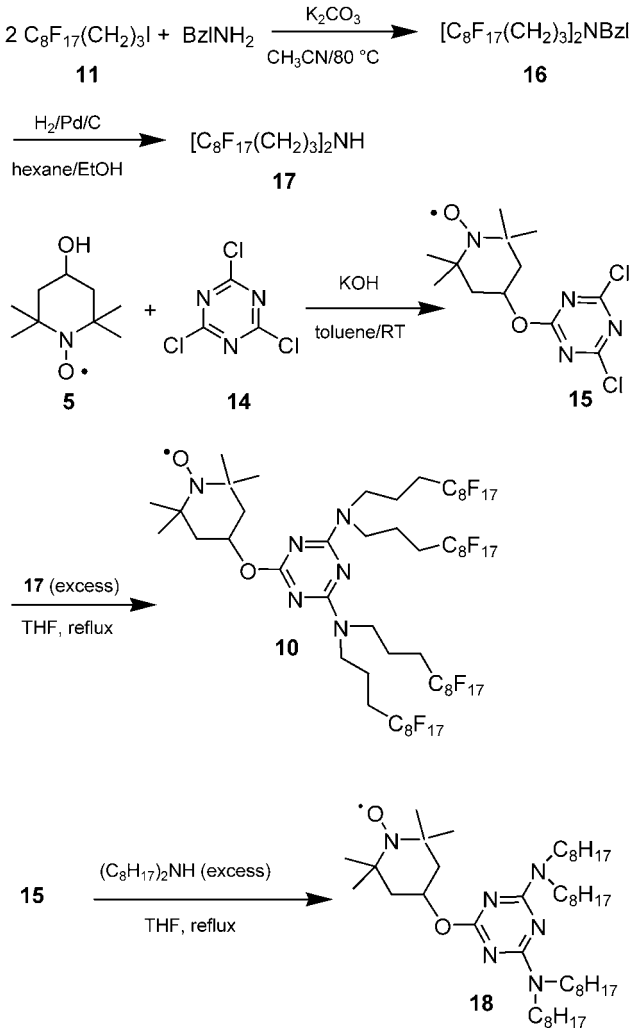


Figure 1. Light fluorous TEMPO radicals.



Scheme 1.



Scheme 2.

are crucial to enhance the affinity for the fluorous phase, the TEMPO radicals **9** (F = 59.9%) and **10** (F = 60.0%) bearing two and four R_F, respectively, were also synthesized.

4-Amino-TEMPO (**8**) was reacted with an excess of 3-(*n*-perfluorooctyl)propyl iodide (**11**)[28] in boiling CH_3CN in the presence of K_2CO_3 as a base (Scheme 1). Although efficient dialkylation of certain primary amines has been achieved under similar conditions,[29] many primary amines react with **11** to give secondary amines as the only products.[30] In the present case bis-*N*-alkylation prevailed and the fluorous-tagged TEMPO **9** was obtained as the major reaction product (yield = 50%). It should be noted that also 4-amino-2,2,6,6-tetramethylpiperidine (**12**) was selectively bis-*N*-alkylated at the primary nitrogen, affording **13** in 68% yield. However, our attempts to convert **13** into **9** using standard conditions for the oxidation of 2,2,6,6-tetramethylpiperidine to TEMPO failed.[31]

The nitroxyl radical **10** with four fluorous tags stemming from a triazine core was conveniently synthesized as depicted in Scheme 2. 1,3,5-Trichlorotriazine (**14**) was treated with 4-hydroxy-TEMPO (**5**) in dry toluene at room temperature, in the presence of powdered KOH as a base, to give **15** in 45% yield. This compound had been previously prepared in lower yields following a different procedure.[32] A two-fold excess of fluorous amine **17**, prepared according to a modification of Rábai's method,[33] was then reacted with **15** in boiling THF. The ammonium salt **17** · HCl formed thereby was easily separated by filtration of the cold reaction mixture and neutralized with aqueous NaOH to give **17**, which could be recycled. The radical **10** was recovered in pure form from the liquid phase in 65% yield after flash column chromatography on silica. The non-fluorous triazine-tethered TEMPO derivative **18** was synthesized likewise from **15** and an excess of di(*n*-octylamine).

Despite the similar fluorine content, the fluorous-tagged radicals **9** and **10** showed different affinities for perfluorocarbons, as indicated by partition coefficient measurements between perfluoro-1,3-dimethylcyclohexane (PDMC) and standard organic solvents (Table 1). Whereas **9** is only slightly preferentially soluble in PDMC than in organic solvents, **10** partitions almost completely in the fluorous phase. Fortunately, **10** is also readily soluble in ethers such as *tert*-butyl methyl ether (MTBE) and, at low concentrations, in CH_2Cl_2. This residual affinity for organic solvents increases with the temperature and greatly simplified the search for convenient reaction conditions when **10** was tested as a catalyst in the oxidation of alcohols. The high affinity of **9** for AcOH is in agreement with the basic nature of the nitrogen atom in the 4-position, which is efficiently shielded from the electron-withdrawing perfluoroalkyl substituents thanks to the interposition of $-(CH_2)_3-$ spacers.[34]

Catalytic Activity

The ability of the fluorous-tagged TEMPO radicals (1 mol % with respect to the substrate) to catalyze the

Table 1. Partition coefficients *P* for fluorous-tagged TEMPO radicals **9** and **10** between perfluoro-1,3-dimethylcyclohexane (PDMC) and standard organic solvents.[a]

Organic Solvent	$P\ [\mathbf{X}]_{PDMC}/[\mathbf{X}]_{Org.\ Solv.}$	
	9	**10**
Toluene	3.1	38.0
CH_2Cl_2	1.4	11.3 (12.3)
CH_3CN	14.0	>100 (>100)
CH_3OH	7.0	20.5 (19.3)
AcOH	0.1	14.5 (15.3)

[a] Determined gravimetrically (Method A, Experimental Section). Values determined by UV-Vis spectroscopy (Method B, Experimental Section) in parentheses.

Table 2. Oxidation of 1-octanol to octanal with aqueous NaOCl.[a]

Entry	Catalyst	t [min]	Conversion [%]	Selectivity [%]
1	**1**	15	98	98
2	**2**	15	96	>99
3	**3**	10	>99	98
4	**4**	15	97	>99
5	**9**	15	>99	>99
6[b]	**10**	10	>99	95
7[c]	**10**	10	>99	94
8[d]	**10**	30	95	96
9	TEMPO	10	>99	>99

[a] Reaction conditions: Oxidant/S/C/KBr = 125/100/1/10. T = 0 °C. Solvent = CH_2Cl_2. Selectivity and conversions determined by GC (internal standard method).
[b] T = 20 °C.
[c] Solvent = MTBE.
[d] Solvent = MTBE, bromide-free conditions.

oxidation of alcohols in combination with KBr (10 mol %) and a slight excess of buffered bleach (pH = 8.6) as the terminal oxidant,[12] was first evaluated using 1-octanol as a model substrate (Table 2). The observed activity and selectivity of the fluorous-tagged catalysts in the biphasic system CH_2Cl_2/H_2O were generally similar to those of TEMPO. Conversions higher than 95% were reached in 10–15 minutes, with almost complete selectivity for the aldehyde. However, a small amount of octanoic acid was detected when **10** was employed (entry 6). This cannot be avoided either by using a different solvent such as *tert*-butyl methyl ether (MTBE) (entry 7) or by working under bromide-free conditions (entry 8). It should be noted that, although slightly decreased, the oxidation rate remained high even in the absence of KBr and the same was observed with all the new catalysts. This is quite interesting in view of large scale operations, where bromide-free conditions and the use of MTBE instead of CH_2Cl_2 would be desirable.

Besides aqueous NaOCl, [bis(acetoxy)iodo]benzene (BAIB) and trichloroisocyanuric acid (TCCA) were also tested as stoichiometric oxidants in the model reaction. They were selected not only on the basis of the excellent results obtained with TEMPO, but also to evaluate whether the insertion of fluorous tags could interfere with different regeneration modes of the active oxidizing species. Indeed, TCCA and BAIB play different roles in the oxidation of alcohols catalyzed by TEMPO. TCCA, as well as OCl^- and OCl^-/Br^-, reacts with TEMPO to form an *N*-oxammonium salt, which oxidizes the alcohol to the corresponding carbonyl compound giving the reduced form of TEMPO, the hydroxylamine TEMPOH. The latter is then reoxidized by TCCA to regenerate the oxoammonium cation.[15] BAIB is a mild organic oxidant which is unable to oxidize TEMPO directly, but which regenerates TEMPO from TEMPOH. Dismutation of TEMPO catalyzed by acetic acid issued from the interaction between BAIB and the alcohol then gives TEMPOH and the active oxammonium salt.[14] In both cases the choice of the solvent is crucial. Both TCCA and BAIB afford good results in terms of reaction rates and selectivity for the carbonyl compound when CH_2Cl_2 is used. In the case of BAIB reactions carried out in other solvents, such as MTBE, are sluggish.[14,23] On the other hand, oxidation of alcohols with TCCA/TEMPO to give carboxylic acids has been reported in wet acetone.[15c] The behavior of the new catalysts in the presence of these two primary oxidants was thus investigated in CH_2Cl_2

When the fluorous-tagged TEMPO radicals (1 mol % with respect to the substrate) were used in combination with TCCA as the terminal oxidant (Table 3) under anhydrous conditions, reaction rates were similar to those observed with aqueous NaOCl, but overoxidation of 1-octanol to octanoic acid occurred to a larger extent. Such a finding was not particularly surprising, since the oxidation of aldehydes to acids promoted by TCCA can occur also in the absence of nitroxyl radicals.[15c] The addition of a base such as CH_3COONa partly prevents this side-reaction (entries 1 and 3 *vs.* entries 2 and 4),[15a] which had scarce relevance in the TEMPO-catalyzed oxidation of 1-octanol (entry 8). The triazine derivative **10** turned out to be the most selective among the fluorous-tagged catalysts tested (entry 7), while radical **9** afforded large amounts of octanoic acid even in the presence of NaOAc. It should be noted that primary amines are readily oxidized to nitriles by a combination of TCCA and TEMPO.[35] Although the fate of **9** in the oxidation of 1-octanol with TCCA has not been investigated, we suppose that the presence of a tertiary amino group could facilitate degradation of the catalyst, thus enhancing the relative importance of the non-catalyzed TCCA oxidation of the intermediate aldehyde. The nitrogen atoms attached to the triazine ring in **10** are

Table 3. Oxidation of 1-octanol to octanal with TCCA.[a]

Entry	Catalyst	Conversion [%]	Selectivity [%]
1	**1**	93	74
2[b]	**1**	>99	97
3	**2**	95	78
4[b]	**2**	>99	93
5[b]	**3**	>99	86
5[b]	**4**	>99	90
6[b]	**9**	>99	57
7[b]	**10**	>99	98
8	TEMPO	>99	95

[a] TCCA = trichloroisocyanuric acid. Reaction conditions: oxidant/S/C = 105/100/1, T = 0 °C, solvent = CH_2Cl_2. Selectivity and conversions were determined by GC (internal standard method) after a reaction time of 10 min.
[b] In the presence of CH_3COONa (3 mol equiv. with respect to TCCA).

poor electron donors and are much less susceptible to oxidative attack.[36]

The oxidation of 1-octanol with BAIB proceeded slower than with TCCA or bleach independently of the catalyst used, requiring at least two hours to go to completion (Table 4) with a higher catalyst loading (5 mol % with respect to the substrate). This is clearly a consequence of the different reaction mechanism. Overall reaction rates were generally similar to those observed with TEMPO, but it should be noted that rate profiles and selectivities (Figures 2 and 3) were greatly influenced by the nature of the bond connecting the fluorous domain with the rest of the molecule.

Initial reaction rates observed in the presence of the light fluorous radicals **1** – **4** and with **9** were higher than that observed with TEMPO (Figure 2). In particular, **3** and **4** featuring an amido bond gave TOFs at 30 minutes = 0.40 min^{-1} and 0.55 min^{-1}, respectively, against TOF at 30 minutes for TEMPO = 0.15 min^{-1}. Although the oxidation catalyzed by **10** started quite slowly (TOF at 30 minutes = 0.07 min^{-1}), conversion after 2 hours was close to that obtained with TEMPO (Table 4, entries 7 and 9). It is worth noting that the non-fluorous triazine-tethered TEMPO derivative **18** gave TOF at 30 minutes = 0.43 min^{-1} and overall conversion and selectivity similar to that of **10** (Table 4, entries 7 and 8). The induction time observed with **10** is thus related to the heavy fluorous nature of this catalyst, with possible effects in terms of lipophobicity, self-aggregation and formation of micro- and nanophases ("fluorous self-assembly"),[37] and not to its specific design. Finally, the oxidation of 1-octanol catalyzed by **10** proceeded more slowly under fluorous biphasic (FB) conditions (Table 4, entry 6) than in CH_2Cl_2 (entry 7). It has been shown that alcohols are selectively oxidized with oxygen under FB conditions in the presence of catalytic amounts of TEMPO and fluorous copper(I) complexes at 90 °C.[38,39] A single homogeneous phase is formed at such a temperature,[39] overcoming mass transfer limitations. In the present case, the system remained biphasic at room temperature hampering the intimate contact between the fluorous catalyst and the organic species.

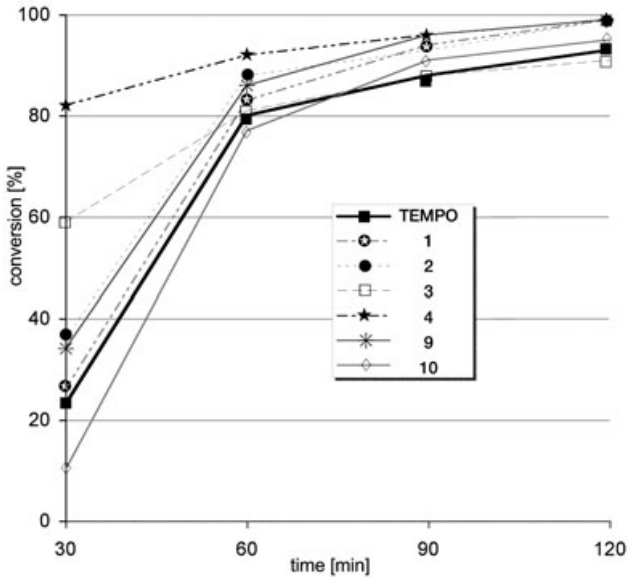


Figure 2. Oxidation of 1-octanol to octanal with BAIB. Conversion profiles for reactions mediated by fluorous-tagged TEMPO radicals.

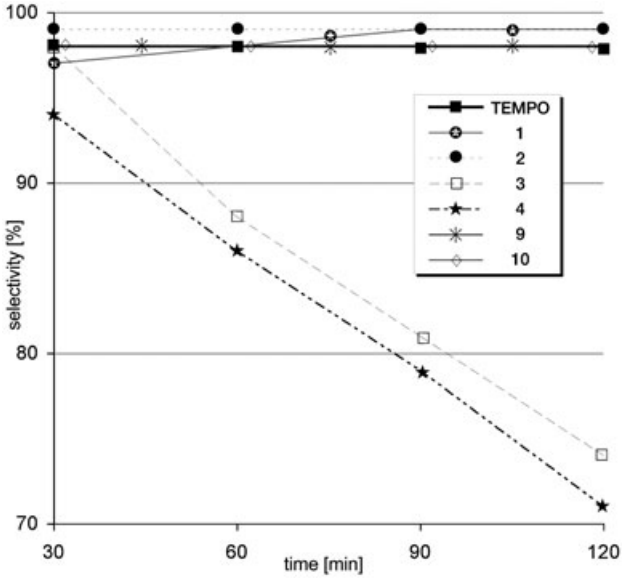


Figure 3. Oxidation of 1-octanol to octanal with BAIB. Selectivity profiles for reactions mediated by fluorous-tagged TEMPO radicals.

As shown in Figure 3, the selectivity for the aldehyde in reactions catalyzed both by TEMPO and fluorous radicals **1**, **2**, **9** and **10** was almost constant in time (> 97%). Radicals **3** and **4** initially afforded good aldehyde selectivities (98% and 94% at 30 minutes for **3** and **4**, respectively), but after 30 minutes formation of octanoic

Table 4. Oxidation of 1-octanol to octanal with BAIB.[a]

Entry	Catalyst	Conversion [%]	Selectivity [%]
1	**1**	> 99	> 99
2	**2**	> 99	> 99
3	**3**	91	74
4	**4**	> 99	71
5	**9**	> 99	98
6[b]	**10**	56	> 99
7	**10**	93	> 99
8	**18**	94	> 99
9	TEMPO	93	> 99

[a] BAIB = [bis(acetoxy)iodo]benzene. Reaction conditions: oxidant/S/C = 110/100/5, T = 20 °C, solvent = CH_2Cl_2. Selectivity and conversions were determined by GC (internal standard method) after a reaction time of 2 h.

[b] Fluorous biphasic (FB) conditions: CH_2Cl_2/PDMC.

acid was observed and selectivities dropped. It appeared that the aldehyde initially formed was partly oxidized by the excess of primary oxidant still present in solution. The acidity of the −NHCO−group, which is enhanced by the presence of the electron-withdrawing perfluoroalkyl chain,[40] could thus influence the outcome of the reaction, as previously found in the NaOCl-promoted oxidation of primary alcohol groups in carbohydrates to carboxylic acids catalyzed by 4-acetamido-TEMPO.[41]

The substrate scope of the fluorous-tagged TEMPO radicals was next evaluated in reactions promoted by aqueous NaOCl or BAIB, the oxidants which gave the best results in the model reaction.

The light fluorous catalysts **1**–**4** behaved quite similarly in the presence of NaOCl, affording fast and selective oxidation of primary, secondary and benzylic alcohols to their corresponding carbonyl derivatives. All reactions were carried out at 0 °C in the presence of 1 mol % of catalyst and 1.25 mol. equivs. of terminal oxidant with respect to the substrate. Under these conditions, most alcohols were quantitatively oxidized within 15 min, as found in the case of 1-octanol. Selected data for **1** and **3** are reported in Table 5 (entries 1–8). The solubility of radical **10** in CH_2Cl_2 is strongly affected by the temperature, thus NaOCl oxidations were performed at 20 °C in order to dissolve the radical in the organic layer (Table 5, entries 9–14). Oxidation of primary, benzylic and cyclic secondary alcohols proceeded almost quantitatively in only 10–15 minutes. However, as previously demonstrated in the case of TEMPO,[12] reactions were slowed down by increasing the temperature and this is clearly shown by the relatively low conversions achieved when secondary alcohols were oxidized (Table 5, entries 11, 12 and 14). Longer reaction times failed to give complete conversion of those substrates (entry 14) due to the progressive bleaching of the catalysts. Indeed, in the presence of buffered NaOCl/KBr the stability of the active oxoammonium species at 20 °C is much lower than at 0 °C.[12] A number of techniques complementary to the classic FB approach have been developed in the last few years, providing new options for separating fluorous molecules from reaction mixtures.[42] Selective retention of fluorous-tagged molecules on fluorous reverse phase silica gel (fluorous solid-phase extraction, F-SPE)[43] has found widespread application for quick separations of mixtures involving fluorous reagents and scavengers,[44] including light fluorous ones, and is now attracting increasing attention in the field of fluorous catalysis.[45] The separation and recovery of the fluorous-tagged TEMPO derivatives by F-SPE was investigated for the oxidation of cycloctanol with aqueous NaOCl. After completion of the reaction the aqueous layer was discarded and the organic solution was loaded onto a commercially available fluorous reverse phase silica gel cartridge. Cyclooctanone was eluted with a small amount of CH_3CN, an organic solvent showing little affinity for fluorous compounds, and recovered after evaporation of the solvent (Table 5, entries 4, 8 and 13). Isolated yields of about 80% were obtained, which are somewhat lower than GC yields. This is due to a partial loss of the volatile product during the final evaporation of CH_3CN under reduced pressure. The light fluorous radical **1** and the heavy fluorous radical **10** were retained selectively as an orange band at the top of the cartridge, whereas the light fluorous radical **3** moved down, although slower than cyclooctanone. Indeed, the reaction product was free from any fluorous residue as shown by

Table 5. Oxidation of alcohols to carbonyl compounds with aqueous NaOCl.[a]

Entry	Catalyst	Substrate	Product	t [min]	Conversion [%][b]	Selectivity [%]
1	**1**	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	10	>99	98
2	**1**	1-Undecanol	Undecanal	15	>99	98
3	**1**	2-Octanol	2-Octanone	15	91	98
4	**1**	Cyclooctanol	Cyclooctanone	15	99 (80)	>99
5	**3**	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	10	>99	>99
6	**3**	1-Undecanol	Undecanal	15	>99	98
7	**3**	2-Octanol	2-Octanone	15	>99	>99
8	**3**	Cyclooctanol	Cyclooctanone	15	>99 (77)	>99
9	**10**[c]	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	10	>99	97
10	**10**[c]	1-Undecanol	Undecanal	15	96	98
11	**10**[c]	2-Undecanol	2-Undecanone	30	95	>99
12	**10**[c]	2-Octanol	2-Octanone	15	92	>99
13	**10**[c]	Cyclooctanol	Cyclooctanone	15	99 (81)	>99
14	**10**[c]	1-Phenylethanol	Acetophenone	15	77	>99
				60	92	
				120	97	

[a] Reaction conditions: see Table 2.
[b] Isolated yields in parentheses.
[c] $T = 20$ °C.

the absence of signals in the ^{19}F-NMR. By a simple solvent switch to Et_2O, it was possible to recover **1** (89% of the starting material) and **10** (75%), although not quantitatively. Recycling of these catalysts was attempted (Table 6), with moderate success in the case of **10** but less satisfactorily with **1**. The sudden drop in catalytic activity observed with **1** can be accounted for by the catalyst undergoing degradation, since the orange color characteristic of TEMPO derivatives disappeared during the second run. In the case of **10**, the high fluorophilicity of this compound allowed us to compare F-SPE to another fluorous quick work-up method, namely liquid-liquid extraction of the reaction mixture with a perfluorocarbon (F-LLE). As reported in Table 6, F-LLE of the organic phase containing cyclooctanone with PDMC afforded better results than F-SPE. In the first three runs, 95%, 96% and 100% of the fluorous catalyst introduced was recovered, respectively. Only in the fourth run was an evident decrease of catalytic activity observed, matched by a loss of recovered catalyst (83%).

Table 6. Recycling of F-tagged TEMPO: oxidation of cyclooctanol with NaOCl.[a]

Run	Catalyst	Method[b]	Conversion [%]	Selectivity [%]
1	**1**	F-SPE	99	>99
2			60	>99
1	**10**[c]	F-SPE	99	>99
2			84	>99
3			63	>99
1	**10**[c]	F-LLE	99	>99
2			90	>99
3			83	>99
4			64	>99

[a] Reaction conditions: see Table 2. Reaction time = 15 min.
[b] F-SPE = fluorous solid phase extraction; F-LLE = fluorous liquid-liquid extraction.
[c] $T = 20\,^{\circ}C$.

The use of readily available, easy to handle and low toxic trivalent iodine reagents such as BAIB is particularly appealing for small-scale oxidation of alcohols because of the high yields and chemoselectivities obtained under mild reaction conditions.[46] Moreover, most oxidation procedures developed for BAIB and related compounds have been extended to polymer-supported hypervalent iodine reagents which can be recovered by filtration and then regenerated.[47] In this context, there is a strong interest for easily removable and possibly recyclable TEMPO derivatives able to catalyze BAIB oxidations. The oxidation of representative alcohols with BAIB in CH_2Cl_2 was thus investigated at 20 °C in the presence of 5 mol % of fluorous catalyst and 1.1 mol equivs. of terminal oxidant with respect to the substrate (Table 7). On the basis of the preliminary experiments with 1-octanol and the results obtained with aqueous NaOCl, only **1** was tested among the light fluorous radicals available.

The amount of fluorous radicals (**1**, **9**, or **10**) used in BAIB-promoted oxidations was lower than that generally used in similar reactions catalyzed by TEMPO (10 mol %).[14] Nevertheless, primary and benzylic alcohols were smoothly oxidized to the corresponding aldehydes in 2 hours (Table 7, entries 1, 2, 4–6, 9–12). The oxidation of secondary alcohols (entries 3, 4, 7, 8, 13–

Table 7. Oxidation of alcohols to carbonyl compounds with BAIB.[a]

Entry	Catalyst	Substrate	Product	*t* [h]	Conversion[b] [%]	Selectivity [%]
1	**1**	1-Undecanol	Undecanal	2	>99	98
2	**1**	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	2	>99	98
3	**1**	2-Octanol	2-Octanone	6	98	98
4	**1**	Cyclooctanol	Cyclooctanone	6	96	98
5	**9**	1-Undecanol	Undecanal	2	>99	>99
6	**9**	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	2	>99	>99
7	**9**	2-Octanol	2-Octanone	6	46[c]	>99
8	**9**	Cyclooctanol	Cyclooctanone	6	69[d]	>99
9	**10**	1-Undecanol	Undecanal	2	>99 (80)	>99
10[e]	**10**	4-Bromobenzyl alcohol	4-Bromobenzaldehyde	2	>99 (97)	>99
11	**10**	Benzyl alcohol	Benzaldehyde	2	>99	>99
12	**10**	Cinnamyl alcohol	Cinnamaldehyde	2	>99	76
13	**10**	2-Octanol	2-Octanone	24	92	>99
14[e]	**10**	Cyclooctanol	Cyclooctanone	14	91 (78)	>99
15[e]	**10**	2-Undecanol	2-Undecanone	24	83	>99
16[e]	**10**	1-Phenylethanol	Acetophenone	6	93 (88)	>99

[a] Reaction conditions: see Table 4.
[b] Isolated yields in parentheses.
[c] Conversion at 12 h = 51%
[d] Conversion at 12 h = 73%
[e] Using catalyst **10** recovered from the reaction summarized in the previous entry.

16) proceeded more slowly, the reaction rates depending on the steric hindrance of the substrate analogously to what was found with TEMPO.[15] In addition, the oxidation of secondary alcohols was found to be quite sensitive to the nature of the fluorous catalyst employed: nearly quantitative conversions of 2-octanol and cyclooctanol were achieved in 6 hours in the presence of the light fluorous TEMPO **1** (entries 3, 4), whilst the oxidation of the same alcohols proceeded sluggishly in the presence of the 4-amino-substituted TEMPO **9** (entries 7, 8). After an initial induction time, the heavy fluorous radical **10** gave slow but steady reactions (entries 13 and 14). It is worth noting that **10** isolated in a few minutes by F-LLE of the reaction mixture containing 2-octanone (entry 13) could be successfully reused (entry 14). This recovery/recycling process was sequentially applied (entries 14–16), allowing the oxidation of other secondary alcohols to the corresponding ketones in good yields. The quick separation of the catalyst also simplified the recovery of the products, which were isolated pure after column chromatography using a short pad of silica gel. Recovery/recycling of radicals **1** and **9** after F-SPE of the reaction mixture was also possible, but less efficient, as shown in the case of the oxidation of 1-octanol (Table 8).

Thanks to the milder oxidizing environment, the service lifetime of radical **1** in BAIB-promoted reactions is longer than that of the same radical in the presence of aqueous NaOCl. However, degradation of **1** (and **9**) still occurs, thus limiting the number of recycles. This can be improved by choosing a different fluorous-tagged TEMPO radical such as **10**, which was recovered by F-LLE (98% of the introduced amount for each recovery) and reused five times with a minor loss of catalytic activity observed in the 6th run (Table 8).

Table 8. Recycling of F-tagged TEMPO: oxidation of 1-octanol with BAIB.[a]

Run	Catalyst	Method[b]	Conversion [%]	Selectivity [%]
1	**1**	F-SPE	>99	>99
			>99	>99
			81	91
			21	40
1	**9**	F-SPE	>99	98
			>99	98
			72	55
1	**10**	F-LLE	93	>99
			92	>99
			93	>99
			87	>99
			91	98
			85	98

[a] Reaction conditions: see Table 4. Reaction time = 2 h.
[b] F-SPE = fluorous solid phase extraction; F-LLE = fluorous liquid-liquid extraction.

Conclusion

Fluorous-tagged TEMPO derivatives synthesized from easily available precursors were used as catalysts for the oxidation of a variety of alcohols under mild conditions, affording results very similar to those obtained with TEMPO. Reactions were performed in conventional organic solvents under homogeneous or liquid-liquid aqueous-organic conditions, and fluorous separation techniques were applied to isolate the fluorous-tagged radicals from the organic products. Promising results were obtained using popular primary oxidants such as aqueous NaOCl and, in particular, BAIB. With the latter, the heavy fluorous radical **10** could be reused up to six times in the oxidation of 1-octanol showing only minor loss of catalytic activity. The new fluorous-tagged radicals thus share the advantages usually associated with the use of polymer-supported TEMPO derivatives (simplified work-up procedures, quick recovery, recyclability) without some of their common limitations (lack of versatility, mass transfer limitations, poor accessibility to the active site). Results obtained in the present work are also intended to provide further guidelines for the rational design of fluorous-tagged stable nitroxyl radicals and for the development of all-fluorous catalytic systems. In this context, the combination of fluorous-tagged TEMPO derivatives with a recyclable fluorous version of BAIB[48] and the use of molecular oxygen as the primary oxidant are worth investigating.

Experimental Section

General Remarks

Solvents were purified by standard methods and dried if necessary, except perfluoro-(1,3-dimethyl)cyclohexane (Apollo Scientific Ltd., UK) that was used as received. 4-Hydroxy-TEMPO (**5**) pentadecafluorooctanoyl chloride (**6**), 4-amino-TEMPO (**8**) were purchased from Sigma-Aldrich and used as received. 3-(*n*-Perfluorooctyl)propionyl chloride (**7**),[27] 3-(*n*-perfluorooctyl)propyl iodide (**11**),[28] and the fluorous-tagged TEMPO **1** were prepared as described in the literature.[26] Fluorous amine **17**,[33,34] and triazine-tethered TEMPO **15** are known compounds.[32] The original synthetic procedures have been conveniently modified as described below. Reactions were monitored by TLC on silica gel 60 F_{254}. Column chromatography was carried out on silica gel SI 60 (Merck, Germany), 0.063–0.200 mm (normal) or 0.040–0.063 mm (flash). Fluorous solid phase extraction (F-SPE) on fluorous reverse phase silica gel was carried out on FluoroFlash® SPE cartridges, 5 g, 10 mL (Fluorous Technologies Inc., USA). Melting points (uncorrected) were determined with a capillary melting point apparatus Büchi SMP-20. ^{1}H NMR (300 MHz), ^{13}C NMR (75.4 MHz) and ^{19}F NMR (282 MHz) spectra were recorded in $CDCl_3$ on a Bruker AC 300 spectrometer with tetramethylsilane ($\delta = 0$), $CDCl_3$ ($\delta = 77$) and $CFCl_3$ ($\delta = 0$) as internal standards, respectively. TEMPO derivatives are paramagnetic compounds giving NMR spectra with only broad signals that

are not reported. ElectroSpray ionization (ESI) mass spectrometry: Bruker APEX II ICR-FTMS mass spectrometer (source: nano ESI at 45 °C). FT-IR spectra were recorded on a Perkin Elmer 1725X instrument. GC analyses were performed on an Agilent 6850 instrument (column: HP-1 100% dimethylpolysiloxane 30 m × 320 μm × 0.25 μm); carrier = He (constant flow); mode = split (split ratio = 80:1); injector T = 250 °C; detector (FID) T = 280 °C. The products of the oxidation reactions were determined by comparison with the commercially available carbonyl compounds and carboxylic acids. Elemental analyses: Departmental Service of Microanalysis (University of Milano).

$C_8F_{17}C_2H_4COO$-TEMPO (2)

3-(*n*-Perfluorooctyl)propionyl chloride (**7**; 1.02 g, 2.00 mmol) was dissolved in dry Et_2O and added dropwise to a solution of 4-hydroxy-TEMPO (**5**; 0.31 g, 1.83 mmol) and Et_3N (0.31 mL, 2.23 mmol) in Et_2O (10 mL) at 0 °C. The reaction mixture was stirred at 0 °C for one hour then allowed to warm to room temperature and then stirred overnight. Water (10 mL) was added to the reaction and the organic phase separated, the aqueous phase was extracted twice with Et_2O. The organic phase was washed with water and brine and dried over Na_2SO_4. The solvent was evaporated to leave the crude product which was purified by column chromatography (silica gel, hexane/AcOEt, 4/1) to give the title compound as a pale orange solid; yield: 0.47 g (40%); mp 79–81 °C. IR (KBr, selected data): ν = 1732 (C=O), 1372 (N–O) cm^{-1}; anal. calcd. for $C_{20}H_{21}F_{17}NO_3$ (646.36): C 37.16, H 3.27, N 2.17; found: C 37.06, H 3.25, N 1.78.

C_7F_{15}CONH-TEMPO (3)

Pentadecafluorooctanoyl chloride (**6**; 0.25 mL, 0.99 mmol) was dissolved in dry Et_2O (3 mL) and added dropwise to solution of 4-amino-TEMPO (**8**; 0.16 g, 0.92 mmol) and triethylamine (0.16 mL, 1.12 mmol) in dry Et_2O (3 mL). The reaction mixture was stirred for an hour at 0 °C and then allowed to warm to room temperature and was left stirring overnight. The reaction was quenched with water (5 mL), the organic layer separated and the aqueous layer extracted three times with Et_2O. The combined organic layer was washed with water, brine and dried over Na_2SO_4. The crude amide was purified by column chromatography (silica gel, hexane/Et_2O, 4/1), followed by recrystallization from hexane and Et_2O to give the title compound as a light orange solid; yield: 0.14 g (28%); mp 94–97 °C. IR (KBr, selected data): ν = 3330 (N–H), 1695 (C=O), 1368 (N–O) cm^{-1}; anal. calcd. for $C_{17}H_{18}F_{15}N_2O_2$ (567.31): C 35.99, H 3.20, N 4.94; found: C 36.08, H 3.35, N 5.10.

$C_8F_{17}C_2H_4$CONH-TEMPO (4)

3-(*n*-Perfluorooctyl)propionyl chloride (**7**; 0.51 g, 1.00 mmol) was dissolved in dry Et_2O (3 mL) and added dropwise to solution of **8** (0.16 g, 0.92, mmol) and triethylamine (0.16 mL, 1.12 mmol) in dry Et_2O (3 mL). The reaction mixture was stirred for an hour at 0 °C and then allowed to warm to room temperature and was left stirring overnight. The reaction was quenched with water (5 mL), the organic layer separated and the aqueous layer extracted three times with Et_2O. The combined organic layer was washed with water, brine and dried over Na_2SO_4. The crude amide was purified by column chromatography (silica gel, hexane/Et_2O 4/1) to give the title compound as a light orange solid; yield: 0.16 g (28%); mp 99–102 °C. IR (KBr, selected data): ν = 3309 (N–H), 1651 (C=O), 1367 (N–O) cm^{-1}; anal. calcd. for $C_{20}H_{22}F_{17}N_2O_2$ (645.37): C 37.22, H 3.44, N 4.34; found: C 37.21, H 3.38, N 4.13.

$(C_8F_{17}C_3H_6)_2$N-TEMPO (9)

In a Schlenk tube, a mixture of **8** (0.17 g, 1 mmol), K_2CO_3 (0.43 g, 3 mmol) and 3-(*n*-perfluorooctyl)propyl iodide (**11**; 2.21 g, 3.75 mmol) in dry CH_3CN (10 mL) was stirred under nitrogen for 60 h at 80 °C. The suspension was cooled to room temperature and diluted with Et_2O (30 mL). After filtration of the solid, the solvents were evaporated, and the product was purified by column chromatography (silica gel, hexane/Et_2O, 9/1 to recover the excess of 11, then hexane/Et_2O, 7/3) affording the title compound as an orange solid; yield: 0.54 g (50%); mp 65.5–66.5 °C. IR (KBr, selected data): ν = 2981 (N–H), 1372 (N–O) cm^{-1}; anal. calcd. for $C_{31}H_{29}F_{34}N_2O$ (1091.52): C 34.11, H 2.68, N 2.57; found: C 33.96, H 2.53, N 2.81; HR-MS (ESI): m/z = 1092.18611 ($[M+H]^+$); calcd. for $[C_{31}H_{30}F_{34}N_2O]^+$: 1092.18142.

Fluorous Amine (13)

4-Amino-2,2,6,6-tetramethylpiperidine (**12**; 0.16 g, 1 mmol), K_2CO_3 (0.43 g, 3 mmol) and dry CH_3CN (6 mL) were placed in a flame-dried Schlenk tube under nitrogen. The mixture was stirred for 15 min at room temperature, then 3-(*n*-perfluorooctyl)propyl iodide (**11**; 1.76 g, 3 mmol) was added and the reaction was stirred for 48 h at 60 °C. The suspension was cooled to room temperature and diluted with Et_2O (30 mL). After filtration of the solid, the solvents were evaporated, and the product was purified by column chromatography (silica gel, MTBE) affording the title compound as a white solid; yield: 0.73 g (68%); mp 33–34 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.01 (t, J = 12.2 Hz, 2H), 1.12 (s, 6H), 1.18 (s, 6H), 1.51–1.59 (m, 2H), 1.61–1.75 (m, 4H), 1.98–2.25 (m, 4H), 2.51 (t, J = 6.7 Hz, 4H), 2.89–3.04 (m, 1H); ^{13}C NMR (75.4, $CDCl_3$): δ = 19.8, 28.9, (t, $^2J_{C,F}$ = 21.5 Hz), 35.6, 41.4, 48.9, 51.3, 51.7, 105.0–122.8 (m, R_F); ^{19}F NMR (282 MHz, $CDCl_3$): δ = −126.7 (br s, 4F), −124.3 (br s, 4F), −123.3 (br s, 4F), −122.8 to −121.7 (m, 12F), −114.7 (t, $^3J_{F,F}$ = 14 Hz, 4F), −81.2 (t, $^3J_{F,F}$ = 10.5 Hz, 6 F); anal. calcd. for $C_{31}H_{30}F_{34}N_2$ (1076.53): C 34.59, H 2.81, N 2.60; found: C 34.71, H 2.66, N 2.95.

Triazine-O-TEMPO (15)

A solution of 4-hydroxy-TEMPO (**5**; 0.74 g, 4.24 mmol) in dry toluene (10 mL) was added dropwise at room temperature to a suspension of powdered KOH (0.28 g, 5 mmol) and freshly crystallized 1,3,5-trichlorotriazine (**14**; 0.92 g, 5 mmol) in dry toluene (5 mL). The mixture was stirred for 48 h, then diluted with CH_2Cl_2 (20 mL) and filtered. The liquid layer was washed with water, brine and dried over sodium sulfate. The crude product was purified by column chromatography (silica gel, CH_2Cl_2/MeOH, 98/2) to give the title compound as an orange

solid; yield: 0.61 g (45%). Physical data were in agreement with those reported in the literature.[32]

$(C_8F_{17}C_3H_6)_2NH$ (17)

In a flame-dried Schlenk tube, a mixture of perfluoroalkyl iodide **11** (4.70 g, 8 mmol), K_2CO_3 (1.10 g, 8 mmol) and benzylamine (0.42 mL, 3.85 mmol) in dry CH_3CN (20 mL) was stirred under nitrogen for 30 h at 80 °C. The suspension was cooled to room temperature and diluted with Et_2O (40 mL). After filtration of the solid, the solvents were evaporated, and the product was purified by column chromatography (silica gel, hexane to recover the excess of 11, then hexane/Et_2O 9/1), affording the tertiary amine **16** as a pale yellow oil; yield: 3.58 g (91%). The benzyl group was cleaved by hydrogenolysis as described by Gladysz and co-workers to give the title compound as a white solid; yield: 3.21 g (98%).[34] Physical data of **16** and **17** were in agreement with those reported in the literature.

$[(C_8F_{17}C_3H_6)_2N]_2$-triazine-O-TEMPO (10)

In a flame-dried Schlenk tube, fluorous amine **17** (1.24 g, 1.32 mmol) and triazine-O-TEMPO **15** (96 mg, 0.30 mmol) were dissolved in dry THF (15 mL). The solution was stirred under nitrogen for 6 h at 85 °C, during which a white precipitate (**17**·HCl) was formed. The suspension was cooled to room temperature, diluted with Et_2O (20 mL) and filtered on a Büchner funnel. The solid was washed Et_2O (10 mL) and the combined liquid layers were evaporated to give a thick orange oil. Flash column chromatography (silica gel, petroleum ether/MTBE, 75/25) afforded the pure title compound as an orange solid; yield: 415 mg (65%); mp 73–77 °C. IR (KBr, selected data): $\nu = 1573$, 1525 (C=N), 1366 (N–O) cm^{-1}; anal. calcd. for $C_{56}H_{41}F_{68}N_6O_2$ (2121.86): C 31.70, H 1.95, N 3.96; found: C 32.12, H 1.99, N 3.98; HR-MS (ESI): $m/z = 2144.20114$ ($[M+Na]^+$); calcd. for $[(C_{56}H_{41}F_{68}N_6O_2)Na]^+$: 2144.21027.

$[(C_8H_{17})_2N]_2$-triazine-O-TEMPO (18)

In a flame-dried Schlenk tube, triazine-O-TEMPO **15** (0.16 g, 0.50 mmol) and an excess of dioctylamine (0.56 g, 2.32 mmol) were dissolved in dry THF (3 mL). The solution was stirred under nitrogen for 5 h at 75 °C, then cooled to room temperature and diluted with Et_2O (20 mL). The solution was washed with water, brine and dried over $MgSO_4$. Flash column chromatography (silica gel, CH_2Cl_2) afforded the title compound as a red-orange, thick oil; yield: 204 mg, (65%). IR (KBr, selected data): $\nu = 1568$, 1517 (C=N), 1361 (N–O) cm^{-1}; anal. calcd. for $C_{44}H_{85}N_6O_2$ (730.18): C 72.38, H 11.73, N 11.51; found: C 72.51, H 11.62, N 11.69.

Determination of Partition Coefficients *P*

Method A: A 10-mL vial equipped with a magnetic stirrer was charged with the fluorous-tagged TEMPO radical (25 μmol), perfluoro-(1,3-dimethyl)cyclohexane (2 mL) and the organic solvent (2 mL). The mixture was thermostatted at 25 °C and vigorously stirred for 4 h. A 1-mL sample was taken out of each phase, evaporated to dryness and weighed on an analytical balance. The partition coefficient *P* was determined as the ratio between the weight of the fluorous phase residue and the weight of the organic phase residue.

Method B: A 10-mL vial equipped with a magnetic stirrer was charged with the fluorous-tagged TEMPO radical (8 μmol), perfluoro-(1,3-dimethyl)cyclohexane (2 mL) and the organic solvent (2 mL). The mixture was thermostatted at 25 °C and vigorously stirred for 4 hours. Samples (1 mL) taken out of each phase were diluted 200 times with Et_2O and their UV/Vis absorbance at 226 nm was measured. The concentration of the radical in each phase was determined by comparison with a calibration curve (concentration *vs.* absorbance) previously constructed with known solutions. Partition coefficients P were in good agreement with those obtained with Method A, as shown in Table 1 for radical 10.

Typical Oxidation Procedures

Reactions carried out with fluorous-tagged radicals **1** (NaOCl) and **10** (BAIB) are also illustrative of F-SPE and F-LLE work-up procedures, respectively.

Oxidation of Cycloctanol using Aqueous NaOCl

A 50-mL two-necked, round-bottom flask equipped with a magnetic stirrer and a dropping funnel was charged with cyclooctanol (0.64 g, 5 mmol), radical **1** (28 mg, 0.05 mmol) and CH_2Cl_2 (12.5 mL). To the stirred solution cooled to 0 °C, a 0.50 M aqueous solution of KBr (1 mL, 0.50 mmol) was added, followed by dropwise addition of a 0.35 M aqueous solution of NaOCl (17.8 mL, 6.25 mmol) buffered at pH 8.6 by $NaHCO_3$. The reaction mixture was vigorously stirred for a further 15 minutes. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2×4 mL). The combined organic layers were washed with water (3×5 mL) and dried over $MgSO_4$. The solvent was evaporated under vacuum to leave a residue which was loaded onto a fluorous reverse phase silica gel cartridge and eluted with CH_3CN (6 mL) to isolate cyclooctanone (0.50 g, 80%). The cartridge was then washed with Et_2O (10 mL) to remove the fluorous-tagged catalyst **1** (25 mg, 89%) which was used in a subsequent run (Table 6).

Oxidation of 4-Bromobenzyl Alcohol using BAIB

A water-cooled jacketed vial fitted with a stirring bar was charged with a solution of 4-bromobenzyl alcohol (187 mg, 1 mmol) and *n*-decane (71 mg, 0.5 mmol, internal standard for GC) in CH_2Cl_2 (2 mL). To the stirred solution thermostatted at 20 °C, radical **10** (106 mg, 0.05 mmol) was added, followed by BAIB (0.71 g, 1.1 mmol). After 2 hours the reaction was complete as shown by GC analysis. The solution was extracted with PDMC [perfluoro-(1,3-dimethyl)cyclohexane, 3×2 mL]. The combined fluorous extracts containing **10** were evaporated to dryness under vacuum to recover the fluorous-tagged catalyst **10** (104 mg, 98%) which could be reused without further treatments (Table 8). Pure 4-bromobenzaldehyde (180 mg, 97%) was obtained after elution of the organic layer through a short silica pad (light petroleum ether/CH_2Cl_2, 1/1).

Oxidation of 1-Octanol using TCCA.

A stoppered vial fitted with a stirring bar was charged with a solution of 1-octanol (130 mg, 1 mmol) and *n*-decane (71 mg, 0.5 mmol, internal standard for GC) in CH_2Cl_2 (1 mL). To the stirred solution cooled to 0 °C in an ice-bath, CH_3COONa (258 mg, 3.15 mmol) was added, followed by a solution of radical **4** (6.5 mg, 0,01 mmol) in CH_2Cl_2 (1 mL). After 5 minutes TCCA (244 mg, 1.05 mmol) was introduced and the reaction mixture was stirred for 10 minutes. The mixture was diluted with Et_2O (10 mL), filtered on a PTFE septum and the clear liquid layer was analyzed by GC to determine conversion and selectivity of the reaction.

Acknowledgements

We gratefully acknowledge the European Union (Contract No. HPRN-CT-2000-00002, Development of Fluorous Phase technology for Oxidation processes) for financial support.

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