Self-Terminating Radical Oxygenations: Probing of the Scope of the Concept by Use of Various Organic *O*-Centered Radicals

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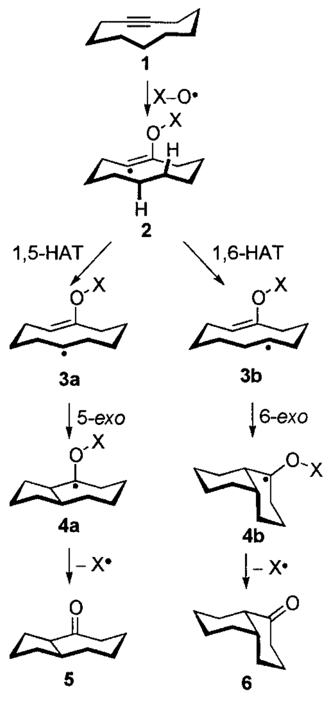
Addition of various organic *O*-centered radicals $XO^{\bullet}$ {i.e. (alkoxycarbonyl)oxyl radicals, $ROC(O)O^{\bullet}$, [(alkoxycarbonyl)acyl]oxyl radicals, $ROC(O)C(O)O^{\bullet}$, (carbamoyl)oxyl radicals, $R_2NC(O)O^{\bullet}$, alkoxyl radicals, $RO^{\bullet}$, and nitroxyl radicals, $R_2NO^{\bullet}$} to alkynes initiates an oxidative radical cyclization cascade, which is terminated by release of a *C*- or *N*-centered radical $X^{\bullet}$. This finding clearly highlights the generality of the recently discovered concept of self-terminating radical oxygenations, through which $C{\equiv}C$ triple bonds may be converted into carbonyl groups under very mild reaction conditions.

Introduction

A wide variety of useful organic transformations involve *O*-centered radicals.[1] Autoxidation processes with molecular oxygen, which involve the formation of peroxyl and alkoxyl radicals as intermediates, are of significant importance for the industrial synthesis of several bulk chemicals. Besides this, the chemical behavior of alkoxyl radicals has been especially intensively studied, and their addition to $C{=}C$ double bonds is a very versatile reaction for formation of $C{-}O$ bonds. In particular, *intra*molecular processes (radical cyclizations), which generally proceed with excellent stereoselectivities, are widely used for the synthesis of oxygen-containing heterocycles.[2,3]

In contrast to this, *inter*molecular addition reactions of *O*-centered radicals to $C{\equiv}C$ triple bonds have as yet received considerably less attention.[4–6] We recently introduced the novel concept of "self-terminating radical oxygenations", which are initiated by intermolecular addition of *O*-centered radicals, $XO^{\bullet}$, to alkynes (for X see below).[7] The basic mechanism of these radical cyclizations is outlined in Scheme 1 for the representative reaction of the medium-sized cycloalkyne **1**. The vinyl radical **2**, formed after initial addition of $XO^{\bullet}$, undergoes an intramolecular hydrogen atom transfer (HAT), **2** → **3a/b**, followed by intramolecular radical addition to the $C{=}C$ double bond, **3a/b** → **4a/b**, and a final homolytic fragmentation of the labile $O{-}X$ bond to yield the ketones **5** and **6** and a radical $X^{\bullet}$ as leaving group.[8] Thus, $XO^{\bullet}$ can be formally regarded as an O atom synthon.



Scheme 1

The term "self-terminating" describes the fact that, so far, the various $X^{\bullet}$ species under investigation [$X^{\bullet}$ = $NO_2^{\bullet}$,[9–11] $SO_3^{\bullet-}$,[12] $H^{\bullet}$,[13] $RC^{\bullet}(O)$[14]] have never been found to react with the alkyne in a chain-propagation step. We have shown that the termination of this cyclization cas-

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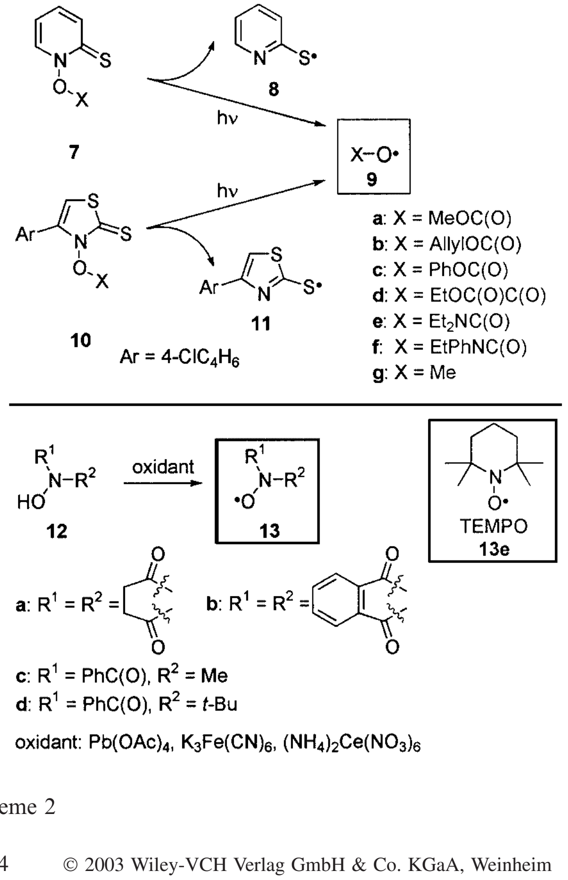
cade is kinetically controlled and determined by the ease of the final homolytic cleavage of the O−X bond.[15]

Encouraged in particular by the finding that the highly unstable acyloxyl radicals RC(O)O• initiate and undergo self-terminating radical oxygenations with excellent yields,[14] we decided to explore the generality of this concept thoroughly. In this work we wish to report on the reactions of the various organic,[16] *O*-centered radicals outlined in Scheme 2 − (alkoxycarbonyl)oxyl radicals (**9a−c**), [(alkoxycarbonyl)acyl]oxyl radicals (**9d**), (carbamoyl)oxyl radicals (**9e/f**), alkoxyl radicals (**9g**), and nitroxyl radicals (**13a−e**) − with cyclodecyne **1**, which was taken as a model system.[17,18]

In comparison with acyloxyl radicals, the tendency of (alkoxycarbonyl)oxyl radicals to undergo decarboxylation is less pronounced, but they are significantly more reactive with regard to intermolecular HAT and addition to π systems.[19−24] In contrast to this, [(alkoxycarbonyl)acyl]oxyl radicals are known to undergo two stepwise, very fast decarboxylations,[25] and they are very versatile precursors for alkoxycarbonyl and alkyl radicals.[26−29] To the best of our knowledge, however, their addition to π systems prior to decarboxylation has not yet been reported. Similarly, due to their rapid decarboxylation,[19,25] (carbamoyl)oxyl radicals are frequently used as precursors for *N*-centered radicals.[30−34] Nitroxyl radicals are comparatively stable compounds and are widely applied as radical traps for mechanistic studies[6,35,36] or used in synthesis in, for example, free-radical "living" polymerizations.[37]



Scheme 2

Results and Discussion

The synthetic route to the radicals used in this work is outlined in Scheme 2. Compounds **9a−g** were generated by photolysis of the corresponding Barton esters **7** or, in part, the respective thiazolethione **10** in acetonitrile in the presence of cycloalkyne **1**. Because of the instability of **7a−d**, these compounds were prepared in situ and used immediately, as described in the literature.[15,38] The nitroxyl radicals **13a−d** were generated from the corresponding hydroxylamines **12**[39,40] by one-electron oxidation (see below). Reaction analysis was accomplished by GC and GC-MS, and the products were identified by comparison both of GC retention times and of NMR spectra with those of authentic samples and with literature data.[9]

Reactions of (Alkoxycarbonyl)oxyl, [(Alkoxycarbonyl)acyl]oxyl, (Carbamoyl)oxyl, and Alkoxyl Radicals 9a−g with 1

The experimental conditions and results of the reactions between the radicals **9a−g** and **1** are compiled in Table 1.

Table 1. Experimental conditions and results from the reactions between (alkoxycarbonyl)oxyl, [(alkoxycarbonyl)acyl]oxyl, (carbamoyl)oxyl, and alkoxyl radicals **9a−g** and cyclodecyne **1**

Entry	Radical precursor	[mM]	**1** [mM]	Yield (%) **5**+**6**[a]
1	**7a**	3.9	12.5	94[b]
2	**7a**	5.9	11.0	86[b]
3	**7a**	7.8	7.6	63[b]
4	**10a**	2.6	9.0	52[b]
5	**10a**	4.6	4.4	16[b]
6	**7b**	3.9	12.4	89[b]
7	**7c**	3.9	12.1	72[b]
8	**7d**	3.9	11.4	82[b]
9	**7e**	4.5	10.0	89[b]
10	**7e**	3.0	10.0	69[c]
11	**7f**	3.0	11.0	58[b]
12	**10g**	3.1	9.8	32[b]

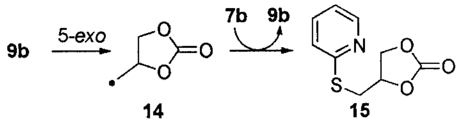
[a] Yield with regard to the minor compound. [b] Combined yield determined by GC with *n*-hexadecane as internal standard. [c] Preparative scale, isolated yield (see text).

Formation of the ketones **5** and **6** was observed in all cases, which is in accordance with the mechanism outlined in Scheme 1 with X• = ROC•(O), ROC(O)C•(O), $R_2NC^•(O)$, and R•, respectively.[41] No reaction between **1** and the radical precursors **7** or **10**, respectively, occurred in the absence of light.

After use of the reaction between **9a** and **1** to optimize the conditions, it turned out that the reaction outcome was clearly influenced by the concentration ratio of radical precursor and cycloalkyne. With the precursor **7a** as the minor compound (ca. 0.3 equiv.), a combined yield of **5** and **6** of over 90% could be achieved (entry 1), whereas use of higher concentrations of **7a** resulted in significantly decreased yields (entries 2 and 3). Thus, with less or no excess of **1**, trapping of radical **9a** by the alkyne presumably could not compete with side reactions, such as decarboxylation or recombination of **9a**.

Comparison of the results given in entries 1, 6, and 7 (Table 1) revealed no explicit dependence of the product yield on the nature of the substituents in **9a−c**. In contrast, it appeared that the reaction outcome was strongly influenced by the type of radical precursor. At present, the reason for the lower yields of **5** and **6** obtained on photolysis of the thiazolethione **10a** in the presence of **1** in comparison with those obtained when **7a** was used as radical precursor (entries 4 vs. 1 or 5 vs. 3, respectively) is not clear.[42]

GC-MS analysis of the irradiated reaction mixture of **7b** and **1** revealed that, besides **5** and **6**, small amounts of an additional product possessing a molecular signal at m/z = 211 were also formed. This signal was assigned to the cyclic carbonate **15**, which is formed after 5-*exo* cyclization of the unsaturated radical **9b** and attack of the resulting carbon radical **14** at **7b** in a chain-propagation step (Scheme 3).[30] Obviously, even with **1** present in threefold excess, this competing intramolecular reaction of **9b** could not be completely suppressed.

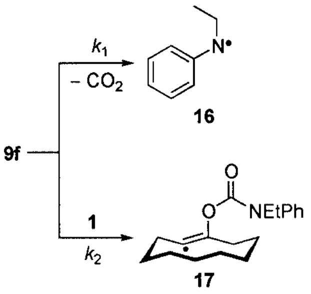


Scheme 3

Although decarboxylation is a comparatively slow process in (alkoxycarbonyl)oxyl radicals,[43] it was essential to ensure that the oxygen atoms in the ketones **5** and **6** did indeed originate from ROC(O)O$^•$ (i.e. **9a−c**) and not from any decarboxylation product RO$^•$. The alkoxyl radical **9g** was therefore independently generated from precursor **10g** and treated with **1**. Although the ketones **5** and **6** were also formed in this reaction, the combined GC yield of only 32%, in comparison with the 52% obtained in the reference reaction of **9a** (entry 12 vs. 4), clearly indicated that (alkoxycarbonyl)oxyl radicals are trapped by the cycloalkyne prior to decarboxylation.[44] However, this experiment unequivocally revealed that even alkoxyl radicals can be employed, although with less efficiency, in self-terminating radical oxygenations, with reactive alkyl radicals acting as the leaving group X$^•$.

The reaction between the [(alkoxycarbonyl)acyl]oxyl radical **9d** and **1** results in the formation of the ketones **5** and **6** in very good yield (entry 8). Clearly, this addition must be faster than the stepwise decarboxylation of **9d**, through which only *C*-centered radicals are formed.[45]

Although the ketones **5** and **6** were also formed in the reactions between (carbamoyl)oxyl radicals (**9e** and **9f**, respectively) and **1**, a strong dependence of the reaction efficiency on the substitution pattern at the nitrogen atom in **9e** and **9f** was apparent. Whereas the combined yield of **5** and **6** was 89% in the case of the *N*,*N*-dialkylated species **9e** (entry 9), the yield in the case of the *N*-alkyl,*N*-aryl-substituted radical **9f** was clearly lower (entry 11). We believe that the rate constant of decarboxylation of **9f**, k_1, by which the *N*-centered, stable "benzyl analogue" radical **16** is formed, must be very fast and of the same order of magnitude as the rate constant k_2 for radical addition to **1** resulting in the vinyl radical **17** (Scheme 4).



Scheme 4

On the other hand, because of the lack of similar stabilization at the nitrogen atom, decarboxylation of **9e** might not be that fast, so that this radical can be efficiently trapped by addition to the alkyne triple bond. This result is the first experimental evidence that (carbamoyl)oxyl radicals have a certain, albeit short, lifetime. This is an important finding, since attempts to detect (carbamoyl)oxyl radicals spectroscopically have so far been unsuccessful.[19,34]

All data presented so far were obtained from experiments performed on analytical scales. Scaling up of photochemical reactions is not normally straightforward, because, in contrast to thermal reactions, non-linear increases both in irradiation time and in solvent amount are generally required. In our case, such an attempt resulted in decreasing overall yields and accumulation of polymeric by-products. It turned out that the best way to accomplish photoinduced, self-terminating radical oxygenations on preparative scales is by suitably increasing the number of reaction flasks, each containing ca. 3−4 mM of radical precursor and ca. 10 mM of alkyne, irradiating them simultaneously, and combining them for workup (see Exp. Sect.). The result of this procedure is demonstrated for the reaction of the (carbamoyl)oxyl radical **9e** in entry 10.

Reaction of Nitroxyl Radicals 13a−e with 1

In comparison with the various *O*-centered radicals so far investigated by us, nitroxyl radicals react only very slowly with closed-shell compounds, and study of their behavior towards alkynes seemed to be a challenge. The experimental conditions and results for the reactions between **1** and **13a−e** are listed in Table 2. No reaction was observed between the bulky nitroxyl radical TEMPO (**13e**) and **1** (entry 11). Therefore, in order to reduce the steric hindrance at the radical center, nitroxyl radicals with one or two acyl substituents were examined. Their generation from the parent hydroxylamines **12a−d** required potent oxidizing reagents; procedures using potassium ferricyanide, PFC, (for monoacylated hydroxylamines) or the stronger oxidant lead tetraacetate, LTA, (for diacylated hydroxylamines) have been described in the literature.[39,46,47] Unfortunately, these oxidants appeared not to be suitable for our purposes, as revealed by the reaction between **1** and **12a** and **12c**, shown in entries 1 and 9, respectively. Although in the case of **12c**

Table 2. Experimental conditions and results from the reactions between nitroxyl radicals **13a**−**e** and cyclodecyne **1**

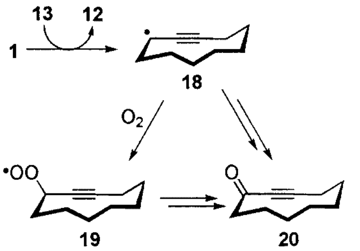
Entry	**12** [mM]	Oxidant[a] [mM]	**1** [mM]	Yield (%) **5**+**6**[b]
1	**a**: 3.1	LTA: 1.2[c]	10.5	8
2	**a**: 10.0	CAN: 10.0[c]	10.0	20[d]
3	**a**: 10.0	CAN: 10.0[c]	10.0	14[e]
4	**a**: 10.0	CAN: 3.0[c]	10.0	18
5	**a**: 3.0	CAN: 10.0[c]	10.0	50[e]
6	**a**: 10.0	CAN: 3.0[c]	10.0	45[e]
7	**b**: 10.0	CAN: 3.6[c]	10.2	27[e]
8	**c**: 10.0	CAN: 3.0[c]	10.2	22[e]
9	**c**: 3.0	PFC: satd.[f]	1.0	no reaction[e]
10	**d**: 10.0	CAN: 3.1[c]	10.2	18[e]
11	**13e**: 62[c]		97.1	no reaction

[a] PFC: $K_3Fe(CN)_6$; LTA: $Pb(OAc)_4$; CAN: $(NH_4)_2Ce(NO_3)_6$. [b] Combined yield determined by GC with *n*-hexadecane as internal standard. [c] In acetonitrile. [d] Under reflux. [e] Ultrasound treatment. [f] Saturated in 2 N aqueous sodium hydroxide/dichloromethane.

the intense blue-green color of the reaction solution indicated immediate formation of the radicals **13c**, the poor mixing of the two-phase solvent system, which could not be improved even by ultrasound treatment, presumably prevented any contact of the radicals with **1**. In the case of LTA-mediated oxidation of **12a**, however, at least small amounts of the ketones **5** and **6** were formed, according to the mechanism in Scheme 1 with $X^• = R_2N^•$, which encouraged us to search for better reaction conditions.

A significant improvement was in the finding that ceric(IV) ammonium nitrate, CAN, which is sufficiently soluble in acetonitrile, smoothly oxidizes the hydroxylamines **12a**−**d** to the respective nitroxyl radicals. After use of the reaction between **13a** and **1** for optimization of the experimental conditions, a satisfactory yield of the ketones **5** and **6** of ca. 50% was obtained when either the oxidant or the radical precursor were used as minor compound (ca. 0.3 equiv.) and the reaction was carried out with ultrasound treatment in the absence of light (entries 5 and 6 vs. 4).[48,49] Neither heating nor ultrasound gave comparable results when all three components were used in equimolar amounts (entries 2 and 3). Similarly, the other nitroxyl radicals **13b**−**d** also underwent this radical oxygenation under the optimized reaction conditions, although with lower efficiency (entries 7, 8, 10).[50]

Besides **5** and **6**, further products were also formed in the reactions between **13a**−**d** and **1**. From the signal intensities in the GC, the major product in all reactions, except that of **13c**, was assigned from its molecular weight of m/z = 150 (determined by GC-MS analysis of the reaction mixtures) as the alkynone **20** (Scheme 5),[51] which may be formed through allylic hydrogen abstraction in **1** by **13**, followed by oxidation.[52−54] This pathway was experimentally verified for the reaction between **1** and **13d**, which, when carried out in an oxygen-saturated solution, gave increased production of **20**, presumably through an intermediate peroxyl radical **19** (data not shown). However, formation of **20** in the reaction between nitroxyl radicals and **1** could not be avoided even with exclusion of oxygen, which indicates that this compound might be also formed through further, as yet unknown pathways.



Scheme 5

Conclusion

We have shown that a large variety of organic *O*-centered radicals $XO^•$ of different stabilities {i.e. (alkoxycarbonyl)oxyl, [(alkoxycarbonyl)acyl]oxyl, (carbamoyl)oxyl, alkoxyl, and also nitroxyl radicals} possess a mechanistically very interesting and yet unknown feature, as they can act as O atom synthons in radical cyclizations of alkynes. The fate of the released *C*- or *N*-centered radicals $X^•$ {i.e. $[ROC^•(O)]$, $[ROC(O)C^•(O)]$, $R_2NC^•(O)]$, $R^•$, and $R_2N^•$, respectively} was not examined, but we have, at least so far, no indication that they also react with the alkyne in a chain-propagation step.

This work is a clear demonstration of the generality of the novel concept of self-terminating radical oxygenations, in which the incoming radical $XO^•$ at the same time provides a relatively unreactive leaving group $X^•$, which is cleaved after the radical cyclization, thus bringing the whole reaction cascade to an end. This reaction allows the oxidative functionalization of alkynes under very mild conditions. Limitations of this methodology arose only in those cases in which serious competition from inter- or intramolecular reactions of the *O*-centered radicals occurred, such as from very fast decarboxylation [in the case of the (carbamoyl)oxyl radical **9f**], from hydrogen abstraction (in the case of the nitroxyl radicals **13a**−**d**), or if the radicals themselves are too unreactive, as is, for example, TEMPO (**13e**).

With this new view on radicals and their properties, we are currently working on the extension of the concept of self-terminating radical cyclizations to other heteroatom-centered radicals.

Experimental Section

General Remarks: NMR spectra were recorded on a Bruker ARX 300 instrument [300 MHz (^1H), 75.5 MHz (^{13}C)] in $CDCl_3$ with use of TMS as internal standard. IR spectra were recorded on a Perkin−Elmer FT-IR 1600 infrared spectrometer. Mass spectra were recorded on a Finnigan MAT 8200 instrument by use of electron ionization (EI) at 70 eV and of chemical ionization (CI) with isobutene as collision gas. Irradiation experiments were carried out in Pyrex reactors (12 mL volume) with use of a medium-pressure mercury lamp. The reaction mixtures were analyzed by GC with *n*-

hexadecane as internal standard. GC: (a) Varian CP 3380; column CP-Sil 5 CB, 30 m, temperature program $100_5 \rightarrow 150 \rightarrow 250_{10}$, heating rates 5 and 10 °C min^{-1}, respectively. GC retention times: 6.2 min (**1**), 9.1 min (**5** and **6**), 17.5 min (*n*-hexadecane); (b) Varian 3400; column Optima 1, 25 m, temperature program $100_5 \rightarrow 150 \rightarrow 250_{10}$, heating rates 5 and 10 °C min^{-1}, respectively. GC retention times: 5.4 min (**1**), 8.0 min (**5** and **6**), 10.4 min (**20**), 16.3 min (*n*-hexadecane). Product identification was carried out by comparison of the GC retention times with those of authentic samples (co-injection) and by GC-MS (EI and CI): Finnigan-MAT 8200, Varian 3700; column Optima 1, 30 m, temperature program $80_5 \rightarrow 250$, heating rate 10 °C min^{-1}.

The Barton esters **7a−d** were unstable and could not be isolated. They were prepared in situ and used immediately (see below) in analogy to a procedure described in the literature.[15,38] The radical precursors **10a** and **10g** were synthesized according to ref.[15] Product identification was performed by comparison both of GC retention times and of NMR spectra with those of authentic samples and literature data.[9]

1-[(*N*,*N*-Diethylcarbamoyl)oxyl]-2(1*H*)-pyridinethione (7e): The sodium salt of *N*-hydroxypyridine-2-thione (1.5 g, 10 mmol) was dissolved under argon in anhydrous benzene (20 mL). With ice cooling, a phosgene solution (20% in toluene, 5 mL) was added dropwise, and the mixture was stirred for 1 h at 0 °C. The reaction flask was protected from light, a mixture of triethylamine (1.0 g, 10 mmol) and diethylamine (0.73 g, 10 mmol) was added, and the reaction mixture was stirred at room temperature for 4 h and hydrolyzed with 25 mL of water. After stirring at room temperature overnight, the mixture was separated. The organic layer was washed with brine and dried, and the solvents were evaporated. The crude residue was purified by crystallization (toluene/cyclohexane, 1:5) to yield **7e** (1.4 g, 62%) as a yellow solid, which appears to be a mixture of two tautomers. Mp. 110−115 °C (dec.). IR (KBr): $\tilde{\nu}$ = 2973, 1756, 1266, 1142 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300.1 MHz): δ = 8.64 (m, 0.1 H), 7.66 (m, 1.9 H), 7.25 (m, 1.1 H), (m, 0.9 H), 3.59 (q, 1.8 H), 3.42 (m, 2.2 H), 1.39−1.15 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 176.3 (s), 151.2 (s), 149.9 (s); 138.7 (d), 136.9 (d), 133.5 (d), 112.2 (d), 43.5 (t), 42.2 (t), 14.0 (q), 12.9 (q) ppm. MS (EI): *m*/*z* (%) = 226 (30), 100 (100), 72 (79). MS (CI): *m*/*z* (%) = 227 (100). HRMS: $C_{10}H_{14}N_2O_2S$ requires 226.07761, found 226.07700; $C_9{}^{13}CH_{14}N_2O_2S$ requires 227.08095, found 227.08040.

1-[(*N*-Ethyl-*N*-phenylcarbamoyl)oxyl]-2(1*H*)-pyridinethione (7f): A phosgene solution (20% in toluene, 5 mL) was dissolved under argon in anhydrous benzene (20 mL). Triethylamine (1.0 g, 10 mmol) and *N*-ethylaniline (1.21 g, 10 mmol) were added to the cooled solution, and the mixture was stirred for 45 min at 0 °C and for 1 h at room temperature. The sodium salt of *N*-hydroxypyridin-2-thione (1.5 g, 10 mmol) was then added in portions with exclusion of light, and the reaction mixture was stirred for 4 h at room temperature. After hydrolysis with 25 mL of water, the solution was stirred at room temperature overnight and separated, the organic layer was washed with brine and dried, and the solvents were evaporated, with the temperature of the water bath not exceeding 25 °C. The crude residue was purified by crystallization (toluene/cyclohexane, 1:5) to yield of **7f** (0.64 g, 23%) as a yellow solid, which appears to be a mixture of two tautomers. Mp. 128−130 °C (dec.). IR (KBr): $\tilde{\nu}$ = 3055, 2993, 1762, 1283, 1142, 759, 697 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.30 (m, 0.1 H), 7.73−7.12 (m, 7.7 H), 6.90 (m, 0.2 H), 6.71−6.50 (m, 1 H), 4.07−3.78 (m, 2 H), 1.49−1.12 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ = 176.5 (s), 151.0 (s), 149.8 (s), 139.5 (d), 138.3 (s), 137.3 (s), 133.4 (d), 131.5 (d), 129.8 (d), 129.6 (d), 129.3 (d), 128.6 (d), 128.3 (d), 128.1 (d), 127.0 (d), 124.9 (d), 124.7 (d), 124.5 (d), 112.2 (d), 47.4 (t), 46.2 (t), 13.5 (q), 13.0 (q) ppm. MS (EI): *m*/*z* (%) = 274 (26), 148 (66), 120 (100). MS (CI): *m*/*z* (%) = 275 (100), 121 (100). HRMS: $C_{14}H_{14}N_2O_2S$ requires 274.07761, found 274.07740; $C_{13}{}^{13}CH_{14}N_2O_2S$ requires 275.08096, found 275.08100.

Reactions between 1 and the unstable Radical Precursors 7a−d (Analytical Scale): In a typical experiment, methyl-, allyl-, or phenylchoroformate or oxalic acid ethyl chloroglyoxylate, respectively (600 μmol) and the sodium salt of *N*-hydroxy-1*H*-pyridine-2-thione (650 μmol) were dissolved in anhydrous benzene (3 mL) and stirred at room temperature in the dark for 1 h. This solution (0.2 mL, 40 μmol) was added to a solution of **1** (18 mg, 120 μmol) in anhydrous acetonitrile (10 mL). Dissolved oxygen was removed by ultrasound treatment for 15 min under a steady flow of argon. The mixture was irradiated under argon for 120 min, filtered, and analyzed by GC.

Reactions between 1 and the stable Radical Precursors 7e, 7f, 10a, and 10g (Analytical Scale): In a typical experiment, the radical precursor (26 μmol) and **1** (12.2 mg, 90 μmol) were dissolved in anhydrous acetonitrile (10 mL), and the oxygen was removed by ultrasound treatment for 15 min under a steady flow of argon. The mixture was irradiated under argon for 120 min, filtered, and analyzed by GC.

Reaction between 1 and 7e (Preparative Scale): Compounds **7e** (54.3 mg, 0.24 mmol) and **1** (109 mg, 0.80 mmol) were dissolved in anhydrous acetonitrile (80 mL), and the mixture was uniformly distributed between eight irradiation tubes. After removal of the oxygen by ultrasound treatment under a steady flow of argon for 15 min, the mixtures were irradiated under argon for 150 min and combined, and the solvent was evaporated. The residue was purified by chromatography (SiO_2, diethyl ether/*n*-pentane, 1:7) to yield **5** and **6** (25 mg, 69%, $R_f = 0.31$).

Reactions between 1 and the Nitroxyl Radicals 13a−d (Analytical Scale): In a typical experiment, **1** (100 μmol) was dissolved in anhydrous acetonitrile (10 mL), and the oxygen was removed by ultrasound treatment for 90 min under a steady flow of argon. The respective hydroxylamine **12** (100 μmol) and CAN (35 μmol) were added, and the reaction mixture was treated with ultrasound in the dark for 120 min under a steady flow of argon. The solvent was removed in vacuo, and the residue was dissolved in diethyl ether, washed with water, filtered, and analyzed by GC.

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[16] Self-terminating radical oxygenations were first observed by us in reactions between alkynes and inorganic *O*-centered radicals [i.e., compounds containing no carbon ($NO_3^{\bullet}$, $SO_4^{\bullet-}$, $HO^{\bullet}$)]; see also ref.[7]

[17] Because of the strong transannular interactions, cycloalkyne **1** has proven to be a very suitable trial horse for study of self-terminating radical oxygenations; see refs.[9−14]

[18] We have recently shown that (alkoxycarbonyl)oxyl radicals, [(alkoxycarbonyl)acyl]oxyl radicals, and alkoxyl radicals induce a similar self-terminating, oxidative radical cyclization upon addition to C≡C triple bonds in medium-sized cycloalkynones; see ref.[15] In contrast to the reaction presented in this work, the initial radical addition is followed by a transannular cyclization to the carbonyl double bond.

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[43] Decarboxylation of $ROC(O)O^{\bullet}$: $k \leq 10^5\ s^{-1}$); $ROC(O)O^{\bullet}$ addition to alkenes: $k \approx 1{-}2{\times}10^9\ \text{M}^{-1}{\cdot}s^{-1}$ (values for room temperature); see ref.[19]

[44] Although the thiazolethiones **10** were not ideal radical precursors for our purposes (see text), they were very suitable for mechanistic studies, because their reduced sensitivity towards light simplified their handling significantly.

[45] [(Aryloxycarbonyl)acyl]oxyl radicals are convenient precursors for *O*-centered phenoxyl radicals generated through stepwise decarboxylation-decarbonylation: [45a] P. M. Lahti, D. A. Modarelli, F. C. Rossitto, A. L. Inceli, A. S. Ichimura, S. Ivatury, *J. Org. Chem.* **1996**, *61*, 1730−1738. [45b] D. A. Modarelli, F. C. Rossito, P. M. Lahti, *Tetrahedron Lett.* **1989**, *30*, 4477−4480. To the best of our knowledge, no similar process has yet been described for [(alkoxycarbonyl)acyl]oxyl radicals.

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[49] Absence of light was essential to avoid generation of $NO_3^{\bullet}$ from CAN through photo-induced electron transfer; see refs.[9,11]

[50] It was verified that no reaction between **1** and the hydroxylamines **12a−d** occurred in the absence of oxidant.

[51] No MS (EI) data for **20** were available in the literature. However, the observed fragmentation pattern of **20** was very similar to that of 5-cyclodecynone measured with the same MS machine (C. Jargstorff, Diploma thesis, Universität Kiel, **2002**), whereas **5** and **6** show a completely different pattern; see ref.[9]

[52] This is a plausible assumption, since the rate constants for hydrogen abstractions by nitroxyl radicals and addition to π-systems are of the same order of magnitude: K. U. Ingold, J. C. Walton, *Landolf-Börnstein, Numerical Data and Functional Relationships in Science and Technology, Group II: Atomic and Molecular Physics, Vol. 18, Suppl. to II/13, Nitrogen-Centered Radicals, Aminoxyl and Related Radicals* (Ed.: H. Fischer), Springer Verlag, Berlin, Heidelberg, New York, London, Paris, Tokyo, Hong Kong, Barcelona, Budapest, **1994**, p. 400, 520.

[53] Nitroxyl radical-mediated oxidation of alkynes to α,β-acetylenic ketones in the presence of oxygen has been reported in the literature: S. Sakaguchi, T. Takase, T. Iwahama, Y. Ishii, *Chem. Commun.* **1998**, 2037−2038.

[54] We have indications that the other major product formed in the reactions between **13b−d** and **1** was an adduct species, possibly resulting from recombination of the nitroxyl radical and the cycloalkyne radical **18**.

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