Self-terminating, oxidative radical cyclizations of medium-sized cycloalkynones with inorganic and organic oxygen-centered radicals of type $XO^{\bullet}$: the reaction pathway depends on the nature of X

Uta Wille * and Christian Jargstorff

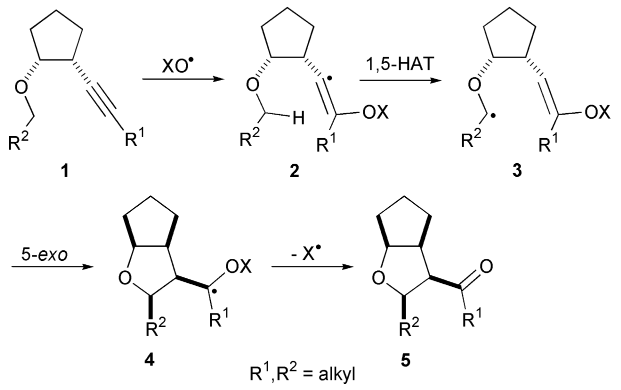
Institut für Organische Chemie der Christian-Albrechts-Universität zu Kiel, Olshausenstr. 40, 24098 Kiel, Germany. E-mail: uwille@oc.uni-kiel.de; Fax: ++49-(0)431-8801558; Tel: ++49-(0)431-8801179

Received (in Cambridge, UK) 18th February 2002, Accepted 8th March 2002
First published as an Advance Article on the web 26th March 2002

The reaction of various inorganic and organic oxygen-centered radicals of type $XO^{\bullet}$ with cyclodec-5-ynone **6** can be used as a mechanistic probe to study the ease with which $X^{\bullet}$ acts as a leaving group in self-terminating, oxidative radical cyclizations. It was observed that when $X^{\bullet}$ has good leaving ability the reaction leads to formation of the bicyclic epoxy ketones **13** and **14**, whereas in the other cases a competition between the individual reversible cyclization steps resulted in predominant formation of the spiro ketone **20**. The experimental data obtained lead to the suggestion that vinyl radicals could rearrange through 1,2-group migrations.

Introduction

In recent publications we reported on a novel concept of self-terminating, oxidative radical cyclizations of cyclic and open-chain alkynes.[1] The proposed mechanism is shown in Scheme 1



Scheme 1

for the exemplary reaction of the alkynyl ether **1**. By intermolecular addition of an oxygen-centered radical of type $XO^{\bullet}$ [with X = NO_2,[2] SO_3^{-},[3] H,[4] RC(O),[5] ROC(O)[6]] at the sterically less hindered site of the C≡C triple bond in **1** a radical cyclization cascade is initiated, which consists of a 1,5-hydrogen atom transfer (1,5-HAT) **2** ⟶ **3**, followed by a 5-*exo* radical cyclization **3** ⟶ **4**. The sequence is terminated by homolytic scission of the O–X bond in **4**, which leads to formation of the anellated tetrahydrofuran **5** in a highly diastereoselective fashion.[2b,c]

Because the released $X^{\bullet}$ is unreactive compared with the entering radical $XO^{\bullet}$, this sequence is of nonchain type and may be considered as a self-terminating, oxidative radical cyclization, since $XO^{\bullet}$ formally acts only as a donor of atomic oxygen. The success of this radical oxygenation was expected to depend on the ease of the homolytic cleavage of the O–X bond in the final step. In the case of $X^{\bullet} = NO_2^{\bullet}$ the activation barrier for the scission was calculated with AM1 methods to be 5.4 kJ mol^{-1}.[2a] It may be assumed that the driving force of this reaction is formation of the stable carbonyl double bond in the product, which counterbalances the energy required for the homolytic fragmentation.

The reaction sequence shown in Scheme 1 is a particular example, as it consists of several consecutive irreversible steps. With the exception of the initial radical addition to the C≡C triple bond, where a reversibility cannot be excluded (see below), both the 1,5-HAT by the reactive vinyl radical **2**, which yields the stabilized α-oxygen radical **3**, as well as the 5-*exo* cyclization of the latter intermediate are expected to be exothermic. The fate of the intermediate **4** should depend on the conditions. Since ring openings in the reversal of 5-*exo* cyclizations are normally slow reactions,[7] **4** could be either stabilized through bimolecular processes, which were never observed under our experimental conditions (*e.g.* radical recombination, disproportionation or hydrogen abstraction), or through fragmentation along the weakest bond. In order to get a deeper insight into the mechanism of these self-terminating radical oxygenations, especially of the final fragmentation step, we decided to study the radical cyclization using a model system with several competing and reversible reaction steps.

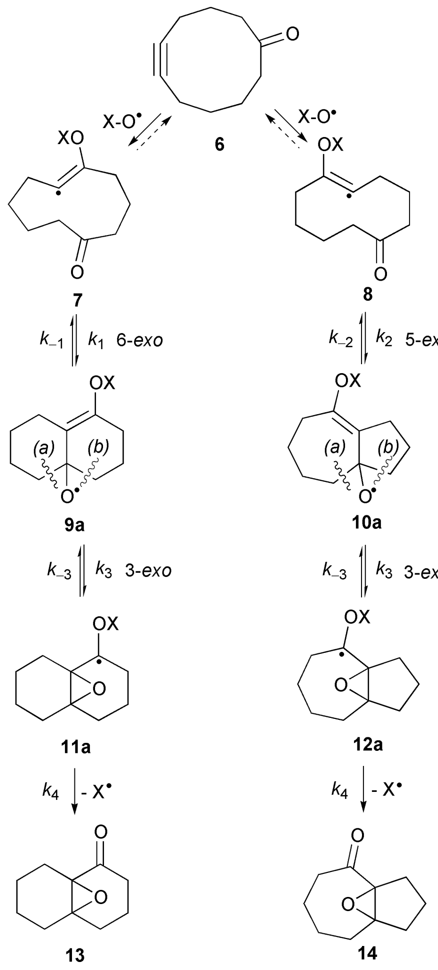
In an earlier work we explored the self-terminating oxidative radical cyclization of medium-sized cycloalkynones induced by electrogenerated $NO_3^{\bullet}$.[2a] The proposed mechanism, which is shown in Scheme 2 (with X = NO_2) for the reaction with cyclodec-5-ynone **6** was different from that of the alkynyl ethers of type **1**, as the initially formed vinylic radicals **7** and **8** did not abstract a hydrogen atom, but instead cyclized to the transannularly activated carbonyl group to yield the allyloxyl radicals **9a** and **10a**, respectively. After a subsequent 3-*exo* cyclization the resulting oxiranylcarbinyl radicals **11a** and **12a** decomposed into $NO_2^{\bullet}$ and the respective epoxy ketones **13** and **14**. These products were formed in a 1.5 : 1 ratio in over 70% combined and isolated yield. This finding was remarkable, since each individual cyclization step in this mechanism should principally be reversible, as may be illustrated by the rate data for the ring closures or respective ring openings, which are compiled in Table 1. The values were either taken from the literature for the unsubstituted parent compounds,[7–9] or for

DOI: 10.1039/b201672a

Table 1 Estimated rate constants in s^{-1} for the reaction steps given in Schemes 2 and 4[a]

k_1	$1 \times 10^{6\,b}$	k_{-1}	$1.1 \times 10^{7\,b}$
k_2	8.7×10^5	k_{-2}	4.7×10^8
k_3	$>4 \times 10^{8\,c}$	k_{-3}	$>4 \times 10^{8\,d}$
k_5	1.1×10^7	k_{-5}	1×10^6
k_6	2.3×10^5	k_{-6}	Not available
k_8	Not observed	k_{-8}	Not available
k_9	4.7×10^8	k_{-9}	8.7×10^5
k_{10}	Not observed	k_{-10}	<70
k_{11}	1	k_{-11}	4.7×10^3
k_{12}	8.3×10^2	k_{-12}	Not available
k_4	$> k_{-3}$	k_7	$<k_{-3}$

[a] The data were taken from ref. 7 unless otherwise stated. [b] Cyclization (and re-opening) of an alkyl radical to C=O double bond; see text. [c] Estimated value; see ref. 8. [d] Ref. 9. [e] Cyclization (and reopening) of alkyl radical to C=C double bond.



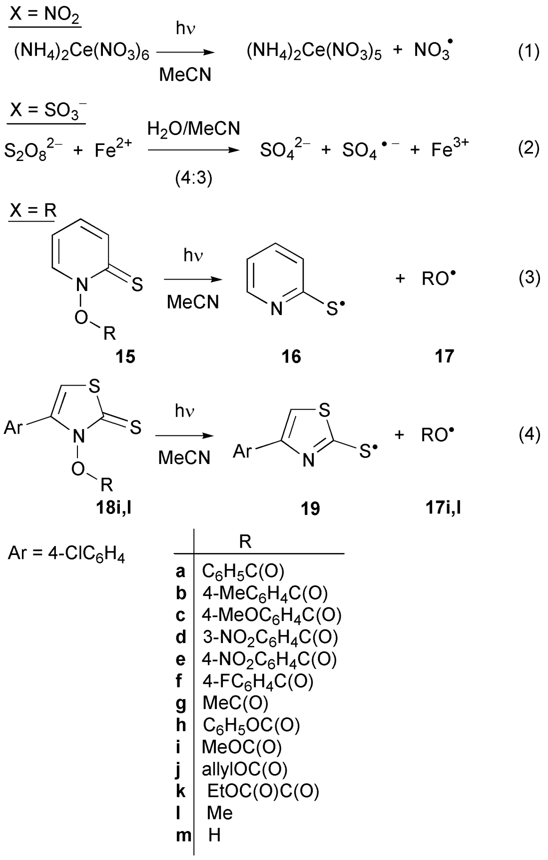
Scheme 2

similar reactions in those cases where no literature data were available, and therefore only a qualitative impression of the rates of the cyclization steps could be obtained. The rate constants for k_1/k_{-1} and k_2/k_{-2}, respectively, are expected to be a lower limit only, since cyclizations of vinyl radicals to π bonds are significantly faster than those of alkyl radicals.[10] However, to our knowledge, the rate constants of vinyl radical cyclizations to carbonyl groups have not been determined to date.

Again, we believe that the key step in the mechanism in Scheme 2 should be the homolytic scission of the O–N bond in the oxiranylcarbinyl radicals **11a** and **12a** to yield $NO_2^{\bullet}$ and **13** and **14**, respectively. The ring opening of unsubstituted oxiranylcarbinyl radicals is a very fast reaction with a rate constant of $k_{-3} > 4 \times 10^8$ s^{-1} (Table 1).[9] The activation barrier of this process was determined to be 25 kJ mol^{-1},[9] thus suggesting a fast oxiranylcarbinyl–allyloxyl radical interconversion.[8] The finding that **13** and **14** were formed in excellent overall yield in the reaction of **6** with $NO_3^{\bullet}$ shows that the final homolytic fragmentation should be an extremely fast process with $k_4 > k_{-3}$, despite the fact that formation of $NO_2^{\bullet}$ is endothermic [heat of formation $\Delta H_f(NO_2^{\bullet}) = 33.08$ kJ mol^{-1}].[11] In this work we want to show that the reaction of **6** with inorganic† and organic oxygen-centered radicals $XO^{\bullet}$ can be used as a very appropriate model system to study the ease of the release of $X^{\bullet}$ in self-terminating radical oxygenations.

Results and discussion

The radicals used in this study were generated according to the reactions shown in Scheme 3. $NO_3^{\bullet}$ was produced through



	R
a	$C_6H_5C(O)$
b	$4\text{-}MeC_6H_4C(O)$
c	$4\text{-}MeOC_6H_4C(O)$
d	$3\text{-}NO_2C_6H_4C(O)$
e	$4\text{-}NO_2C_6H_4C(O)$
f	$4\text{-}FC_6H_4C(O)$
g	MeC(O)
h	$C_6H_5OC(O)$
i	MeOC(O)
j	allylOC(O)
k	EtOC(O)C(O)
l	Me
m	H

Scheme 3 Generation of the radicals $XO^{\bullet}$.

photolysis of cerium(IV) ammonium nitrate (CAN) [eqn. (1)][2d,12] and $SO_4^{\bullet-}$ using the Fenton redox system $Fe^{II}/S_2O_8^{2-}$ [eqn. (2)].[3,13] Acyloxyl radicals $RC(O)O^{\bullet}$ (**17a–g**), (alkoxycarbonyl)oxyl radicals $ROC(O)O^{\bullet}$ (**17h–j**), [(alkoxycarbonyl)acyl]oxyl radicals $ROC(O)C(O)O^{\bullet}$ (**17k**), methoxyl radicals $MeO^{\bullet}$ (**17l**) and hydroxyl radicals $HO^{\bullet}$ (**17m**) were obtained by photolyzing the respective thiopyridones **15**[4–6,14] [eqn. (3)] or thiazolthiones **18**[6,15] [eqn. (4)] (see Experimental section).

The experiments were performed in the case of the reaction of **6** with $NO_3^{\bullet}$ or $SO_4^{\bullet-}$ with equimolar or excess concentrations of the radicals. In contrast to this, the reactions with **17** were performed in the presence of excess **6** (*ca.* three equivalents).‡ This ensured a fast trapping of the extremely reactive radicals through addition to the C≡C triple bond in **6** prior to

---

† Although there is some controversy about the definition “inorganic” for a compound that contains no carbon, this term should be used here for the sake of clarity.

‡ It was ascertained that equimolar amounts of the radicals **17** and the cycloalkynone **6** lead only to a reduction of the total yield but did not affect the product ratio.

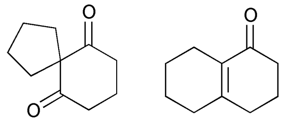
Table 2 Experimental results of the reaction of various radicals XO$^\bullet$ with cyclodecynone **6**

Entry	Radical XO$^\bullet$	$\Delta H_f(X^\bullet)$/kJ mol^{-1}	Yield (%)[a] **13** + **14** + **20**	Product ratio (%)[b]		
				13	**14**	**20**
1	$NO_3^\bullet$	33.08[c]	77	57	43	—
2	$SO_4^{\bullet -}$	Not available	50[d]	43	43	14
3	**17a**	93.78[e]	57[f]	8	4	88
4	**17b**	Not available	93[f]	5	5	90
5	**17c**	19.26 (−50 °C)[g]	80[f]	9	6	85
6	**17d**	Not available	74[f]	29	10	61
7	**17e**	Not available	85[f]	30	11	59
8	**17f**	Not available	88[f]	9	7	84
9	**17g**	−10.00[h]	43[f,l]	6	5	89
10	**17h**	Not available	63[f]	34	15	51
11	**17i**	−167.05[j]	84[f]	12	9	79
12	**17i**		51[i,k]	26	8	66
13	**17j**	Not available	75[f]	18	10	72
14	**17k**	Not available	48[f,l]	17	10	73
15	**17l**	147.79[m]	53[i,k]	49	6	45
16	**17m**	218.00[c]	82[f]	12	6	82

[a] Yield determined by GC using *n*-hexadecane as internal standard. [b] Corrected (see text). [c] Ref. 11. [d] Yield based on consumption of **6**. [e] Ref. 24. [f] Yield with respect to the radical precursor **15**. [g] Ref. 25. [h] Ref. 26. [i] Formation of **21** as minor by-product; see text. [j] Ref. 27. [k] Yield with respect to the radical precursor **18**. [l] Not optimized. [m] Ref. 28.

their decarboxylation in the case of **17a–k**,[5,6] or possible fast side-reactions, *e.g.* β-fragmentation or hydrogen abstraction in the case of **17l,m**.[4,7] The reaction analysis was performed by GC and GC-MS, and the products were identified by comparing their analytical data with literature values[2a,16] and with authentic samples.

An exhaustive analysis of the reaction of **6** with $NO_3^\bullet$ revealed that besides the epoxy ketones **13** and **14** a further oxidation product was also obtained in trace amounts (1%). This compound was identified as the spiro diketone **20**[16] (Fig. 1), which was expected to be formed by photoinduced isomerization of **13**.[17] Interestingly, the thorough reinvestigation of the reaction of **6** with $SO_4^{\bullet -}$ resulted in the finding that besides **13** and **14** compound **20** was also formed, but in only minor amounts (7%). An isomerization of **13** to **20** could be excluded in this case, since the generation of $SO_4^{\bullet -}$ under our conditions (see Scheme 3) required no UV-light. In contrast to this, **20** was identified as the major product in the reaction of the radicals **17** with **6**.§ The results of all experiments are listed in Table 2, in which, due to the photoisomerization of **13** to **20**, the data for the product ratio of **13** : **14** : **20** were corrected in those cases where the radicals were generated by photolysis.¶

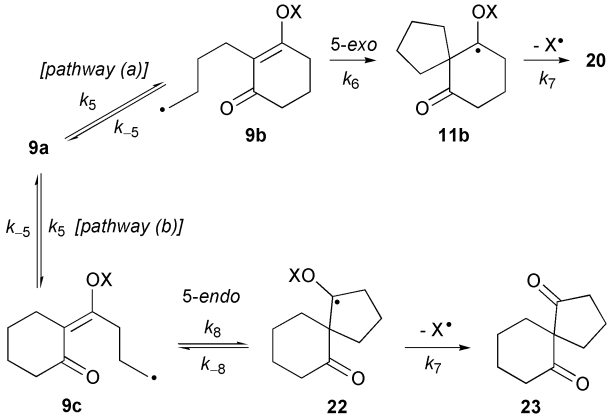


20 **21**

Fig. 1

In the reaction of **17a** (entry 3), **17b** (entry 4), **17c** (entry 5), **17f** (entry 8), **17g** (entry 9) and **17m** (entry 16) the amount of **20** contributed to about 80–90% of the products formed. In the reactions of the other radicals **17** under investigation the fraction of **20** was slightly to significantly smaller with simultaneously increasing amounts of the epoxy ketone **13**. In all reactions of **6** with the radicals **17** compound **14** was unequivocally formed as the minor product. In the case of the reactions of **17g,i,l** the bicyclic α,β-unsaturated ketone **21** (Fig. 1) was also observed as an additional minor by-product, which could originate from solvolysis of **6**.[18]

The formation of **20** could proceed through β-fragmentation in the allyloxyl radical **9a** [according to pathway (a) in Scheme 2], subsequent 5-*exo* cyclization of **9b** and final homolytic cleavage of the O–X bond in the spiro radical **11b** (Scheme 4).



Scheme 4

These observations led to the conclusion that the ability of X$^\bullet$ to act as a leaving group was significantly lower, if X$^\bullet$ = RC$^\bullet$(O), ROC$^\bullet$(O), ROC(O)C$^\bullet$(O), R$^\bullet$ or H$^\bullet$ (see Scheme 3) and that a homolytic fragmentation according to **11a**, **12a** ⟶ **13**, **14** could not compete successfully with the cycloreversion **11a**, **12a** ⟶ **9a**, **10a**, *e.g.* $k_4 < k_{-3}$. Thus, in these cases the reversibility of the cyclization steps in the reaction mechanisms shown in Schemes 2, 4 and 5 became an important factor, and their relative rates determine the product ratio.

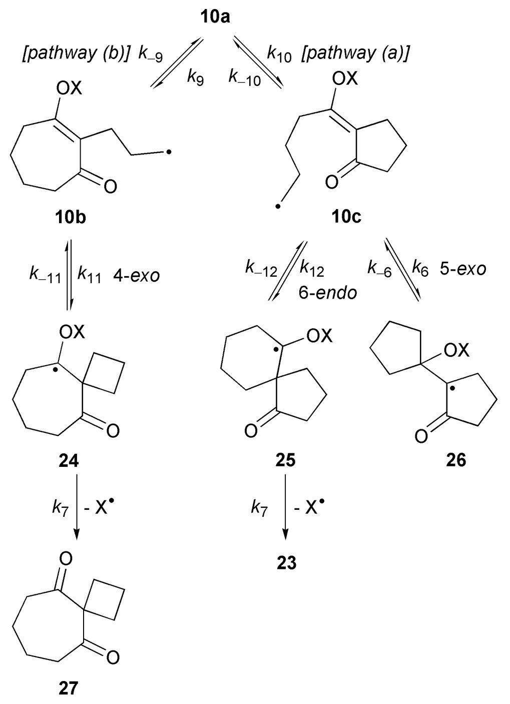
From the rate data in Table 1 it was obvious that the reaction pathway proposed in Scheme 4 for the formation of **20** seemed to be reasonable, since k_5 for the ring opening **9a** ⟶ **9b** suggests a very fast process. Although the reverse ring closure should not be neglected, a 5-*exo* cyclization of the alkyl radical **9b** could occur, which would lead to an irreversible formation of **11b**, since the ring opening of the latter is not very fast.[7] Due to the high dilution (radical concentration 3–4 mM) a radical recombination would be very unlikely, and **11b** could only escape from the whole cyclization cascade by unimolecular homolytic fragmentation to form the carbonyl group in **20** under release of X$^\bullet$.

Interestingly, no products arising from a β-fragmentation of **9a** according to pathway (b) in Scheme 2 were observed. However, as depicted in Scheme 4, the cyclization of the resulting

---

§ We have observed that under our experimental conditions 10% of **13** decayed in 90 min, whereas the isomeric epoxy ketone **14** was stable.

¶ It was verified that no reaction between **6** and **15** or **18**, respectively, occurred in the absence of light.

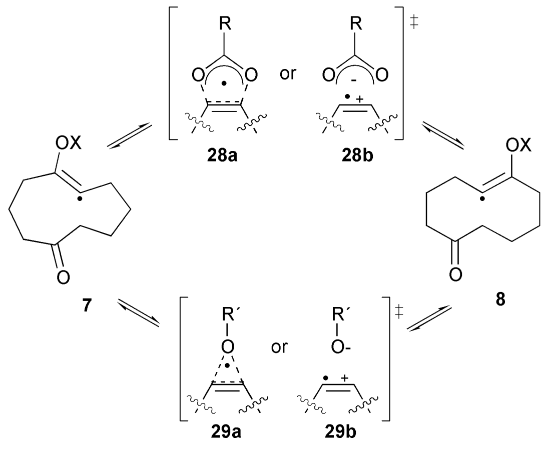


Scheme 5

radical **9c** to the C=C double bond (**9c** ⟶ **22**) should be a 5-*endo* process, which so far has not been observed.[7]

A kinetically unfavorable 4-*exo* cyclization or a slow 6-*endo* process, respectively (see Table 1), could also be the reason, why the spiro ketones **23** and **27**, which would arise from β-fragmentations in **10a** according to either pathway (a) or (b), were not observed (Scheme 5). A usually favorable 5-*exo* cyclization should principally be possible in **10c** to yield an α-carbonyl radical **26**, which should be less stable than its isomer **25**. However, comparison of the rate data for the cyclization and reopening of the respective alkyl radicals k_{10}/k_{-10} (Table 1) led us to the assumption that formation of **10c** from **10a** would also be very slow, so that further reactions of **10c** should be negligible.‖

The nearly equimolar amounts of the epoxy ketones **13** and **14** formed in the reaction of **6** with either $NO_3^{\bullet}$ or $SO_4^{\bullet -}$ reflected the ratio of the primary radical attack, which should occur with approximately the same probability at both sites of the C≡C triple bond, since no apparent steric hindrance exists. It seems reasonable to us that this should also be the case in the reaction of **6** with any radical **17**. However, the generally high combined yield of **13**, **14** and **20** and the absence of any products arising from an initially formed vinyl radical **8** (see Scheme 2) lead to the suggestion that the initial radical addition could also be either completely reversible[19] or that the vinyl radicals **7** and **8** could isomerize, since a direct interconversion **10a** ⟶ **9a** seemed very unlikely. Such an isomerization could possibly proceed through a 1,2-migration (Scheme 6) in analogy to the process in β-(acetoxy)ethyl radicals, which has been extensively described in the literature.[7,20] The transition state could be either five- or three-membered (**28** or **29**, respectively), and both a concerted process with a delocalized radical (structures **a**) or a migration *via* an intimate radical anion–cation pair (structures **b**) could be imagined. However, whereas in the case of X = RC(O), ROC(O) or ROC(O)C(O), respectively, both a five- and three-membered transition state might be considered, the latter



Scheme 6

would be the only possibility if X does not possess a π system, *e.g.* Me or H, respectively.

Which factors actually determine the ease of the final homolytic cleavage leading to the release of $X^{\bullet}$ and formation of the carbonyl group in the ketones **13**, **14** and **20** respectively, should be discussed. Since radical reactions are mostly kinetically controlled processes, the activation barrier for the homolytic dissociation of the O–X bond should be important. Because no data were available for the bond strengths in radicals of type **11** and **12**, the bond dissociation energies must be discussed on the basis of their respective even-electron systems.** As mentioned above, the activation barrier for the O–NO_2 bond cleavage in our systems was calculated to be very low. This is in accordance with the relatively small energy required to cleave an O–N bond in aliphatic nitrates, which is in the range of 160–170 kJ mol^{-1}.[21] In contrast to this, the dissociation of an ester bond of type O–C(O)R requires around 370 kJ mol^{-1},[22] and it may be assumed that the value is very similar in carbonates. The bond strengths in aliphatic ethers are also of a comparable order of magnitude (340 kJ mol^{-1}).[21c] The O–H bond in aliphatic alcohols is still considerably stronger (435 kJ mol^{-1}).[23] With these data in mind, comparison with the results in Table 2 revealed that the ratio of the epoxy ketones **13** + **14** *vs.* spiro ketone **20** reflect the energy of the O–X bond. It may be suggested therefore that homolytic cleavage of an O–S bond and release of $SO_3^{\bullet -}$ should be only slightly more difficult than cleavage of $NO_2^{\bullet}$.††

However, in one case the yield of **13** and **20** appeared to be in the same range (entry 15). The reason is not yet clear, but the observation that cleavage of aroyl radicals bearing an electron withdrawing nitro substituent, leads to a decrease of **20** in favor of formation of **13** (entries 6 and 7 in Table 2), indicated that electronic effects could possibly play a minor additional role, which could lead to a competition between the the 3-*exo* cyclization **9a** ⟶ **11a** and the ring opening **9a** ⟶ **9b**. However, the stability of the released radical $X^{\bullet}$ seemed to be of relatively low importance to the reaction pathway, since the ΔH_f values for $X^{\bullet}$, which are included in Table 2, when they were available in the literature,[11,24–28] did not lead to a satisfying correlation between the yield of **20** and the energy of $X^{\bullet}$.

To conclude, the reaction of **6** with oxygen-centered radicals $XO^{\bullet}$ can be taken as a qualitative measure to determine the general ability of $X^{\bullet}$ as a leaving group in self-terminating, oxidative radical cyclizations. The terminating homolysis of the O–X bond in this sequence is a kinetically driven reaction, which mainly depends on the bond strength of O–X, but not on

---

‖ It should be noted that the radical intermediates **9b**, **9c** and **10b** shown in Schemes 4 and 5 could also cyclize in a fashion, which yields α-carbonyl radicals with a structure related to **26**. However, since these cyclizations would require kinetically unfavorable 4-*exo*, 5-*endo* or slow 6-*endo* processes, respectively, and should lead to less stablized radicals (compared with the α-oxygen radicals **11b**, **22** and **24**), it is very unlikely that they could occur in this reaction.

** However, it might be expected that the energy required for cleavage of the O–X bond in a radical of type $C^{\bullet}(O)$–X is different from that in an even-electron system, but the general trend should be unaffected.

†† No data for the homolytic dissociation of an O–S bond in organic sulfates were available in the literature.

the stability of the released X$^•$. This finding could help us in our ongoing work to discover new reactions of well-known or yet unknown radicals. The inorganic radicals and radical anions $NO_3^•$ and $SO_4^{•-}$, respectively, possess very potent leaving groups X$^•$, which were released at faster rates than the ring opening of an oxiranylcarbinyl radical could proceed thus leading to formation of the epoxy ketones **13** and **14**. Also the organic oxygen-centered radicals RC(O)O$^•$, ROC(O)O$^•$, ROC(O)C(O)O$^•$ and, interestingly, MeO$^•$, as well as the inorganic HO$^•$, were able to induce and undergo a very efficient analogous radical oxygenation. In these cases the terminating homolysis was significantly slower, which leads to a competition between several reversible reaction steps resulting in the final formation of the spiro diketone **20**. However, these results could only be explained by assuming a 1,2-migration of acyloxyl and alkoxyl groups as well as of a hydroxyl moiety in vinylic radicals, which lead to the isomerization of **7** into **8** and *vice versa*.

Experimental

General

NMR spectra were recorded on a Bruker ARX300 instrument [300 MHz (^{1}H), 75.5 MHz (^{13}C)] in $CDCl_3$ using 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 using electron ionization (EI) at 70 eV and chemical ionization (CI) with isobutane as collision gas. The irradiations were carried out in pyrex reactors using a medium-pressure mercury lamp. The reaction mixtures were analyzed by GC with *n*-hexadecane as internal standard. GC: Varian CP 3380, column CP-Sil 5 CB, 30 m, temperature program $100_5 \longrightarrow 200_{15}$, heating rate 5 °C min^{-1}. GC retention times: **6** (10.5 min), **13** (10.9 min), **14** (10.1 min), **20** (11.5 min), *n*-hexadecane (18.0 min). Product indentification was carried out by comparing the GC retention times with authentic samples[2a] (co-injection) and by GC-MS. GC-MS: Finnigan MAT 8200, Varian 3700; column Optima 1, 30 m, temperature program 80 ⟶ 250, heating rate 10 °C min^{-1}.

Synthesis of the radical precursors 15 and 18

The radical precursors **15** and **18** were prepared according to known procedures.[14,15] In the case of known compounds their analytical data were compared with literature values.[14,29]

15c. Mp 127–129 °C (yellow solid from CH_2Cl_2–*n*-pentane); ν_{max}(KBr)/cm^{-1} 3058, 2998, 1765, 1608, 1524, 1452, 1414, 1141 and 1000; δ_H(300 MHz) 2.46 (3 H, s), 6.69 (1 H, dt, *J* 1.8 and 6.9), 7.25 (1 H, ddd, *J* 1.6, 6.8 and 8.8), 7.31 (2 H, m), 7.66 (1 H, ddd, *J* 0.7, 1.8 and 8.8), 7.69 (1 H, ddd, *J* 0.7, 1.8 and 8.8) and 8.13 (2 H, dt, *J* 1.9 and 8.3); δ_C(75.5 MHz) 22.0 (q), 112.7 (d), 122.8 (s), 129.7 (d), 130.8 (d), 133.6 (d), 137.4 (d), 138.1 (d), 146.2 (s), 162.6 (s) and 176.0 (s); *m*/*z* (EI): 245 (M$^+$, 25%), 120 (9), 119 (100) and 91 (33); *m*/*z* (CI): 246 (M$^+$ + H, 33%), 245 (13), 225 (12), 221 (16), 137 (42), 119 (100) and 112 (12); HRMS: $C_{13}H_{11}NO_2S$ requires 245.05106, found 245.05100; $C_{12}{}^{13}CH_{11}NO_2S$ requires 246.05441, found 246.05400.

15d. Mp 121 °C (yellow solid from CH_2Cl_2–*n*-pentane); ν_{max}(KBr)/cm^{-1} 3102, 3075, 3022, 1789, 1606, 1531, 1444, 1410, 1350, 1238, 1224, 1137 and 1014; δ_H(300 MHz) 6.71 (1 H, dt, *J* 1.8 and 6.9), 7.30 (1 H, ddd, *J* 1.6, 6.8 and 8.8), 7.71 (1 H, ddd, *J* 0.7, 1.9 and 6.4), 7.72 (1 H, ddd, *J* 0.7, 1.5 and 7.1), 7.76 (1 H, ddd, *J* 0.5, 7.7 and 8.3), 8.53 (1 H, ddd, *J* 1.1, 2.3 and 8.3), 8.55 (1 H, ddd, *J* 1.1, 1.7 and 7.8) and 9.02 (1 H, ddd, *J* 0.5, 1.6 and 2.2); δ_C(75.5 MHz) 113.0 (d), 125.7 (d), 127.6 (s), 129.2 (d), 130.4 (d), 133.8 (d), 136.3 (d), 137.4 (d), 137.6 (d), 148.4 (s), 160.9 (s) and 175.5 (s); *m*/*z* (EI): 276 (M$^+$, 15%), 167 (8), 150 (100) and 104 (26); *m*/*z* (CI): 277 (M$^+$ + H, 25%), 261 (15), 237 (11), 221 (51), 168 (100), 150 (39) and 112 (47); HRMS: $C_{12}H_8N_2O_4S$ requires 276.02048, found 276.02030; $C_{11}{}^{13}CH_8N_2O_4S$ requires 277.02383, found 277.02360.

15f. Mp 107 °C (yellow solid from CH_2Cl_2–*n*-pentane); ν_{max}(KBr)/cm^{-1} 3052, 1765, 1602, 1525, 1508, 1451, 1414, 1239, 1223, 1139 and 1003; δ_H(300 MHz) 6.67 (1 H, dt, *J* 1.8 and 6.9), 7.16–7.26 (3 H, m), 7.67 (1 H, ddd, *J* 0.7, 1.6 and 5.1), 7.69, (1 H, ddd, *J* 0.7, 1.8 and 7.1) and 8.24 (2 H, ddd, *J* 2.2, 5.3 and 6.9); δ_C(75.5 MHz) 112.7 (d), 116.2 (d), 116.5 (d), 121.9 (s), 133.5 (d), 133.6 (d), 133.7 (d), 137.3 (d), 137.9 (d), 165.1 (s), 168.5 (s) and 175.8 (s); *m*/*z* (EI): 249 (M$^+$, 19%), 123 (100) and 95 (26); *m*/*z* (CI): 250 (M$^+$ + H, 90%), 221 (18), 141 (15), 123 (100) and 99 (19); HRMS: $C_{12}H_8NO_2SF$ requires 249.02599, found 249.02550; $C_{11}{}^{13}CH_8NO_2SF$ requires 250.02933, found 250.02920.

18i. Mp 105 °C (dec., light yellow solid from CH_2Cl_2–*n*-pentane); ν_{max}(KBr)/cm^{-1} 3111, 2951, 1803, 1488 and 1255; δ_H(300 MHz) 3.90 (3 H, s), 6.57 (1 H, s) and 7.40–7.47 (4 H, m); δ_C(75.5 MHz) 53.4 (q), 104.8 (d), 125.8 (s), 129.4 (d), 129.5 (d), 136.6 (s), 139.6 (s), 151.5 (s) and 181.5 (s); *m*/*z* (EI): 301 (M$^+$, 28%), 257 (36), 227 (46), 191 (31) and 168 (100); *m*/*z* (CI): 302 (M$^+$ + H, 3%), 258 (10), 228 (23), 135 (36) and 91 (100); HRMS: $C_{11}H_8NO_3S_2{}^{35}Cl$ requires 300.96341, found 300.96320; $C_{10}{}^{13}CH_8NO_3S_2{}^{35}Cl$ requires 301.96677, found 301.96670; $C_{11}H_8NO_3S_2{}^{37}Cl$ requires 302.96045, found 302.96050.

18l. Mp 121–122 °C (light yellow solid from ethyl acetate–*n*-pentane); ν_{max}(KBr)/cm^{-1} 3298, 2935, 1487 and 1295; δ_H(300 MHz) 3.88 (3 H, s), 6.55 (1 H, s), 7.46–7.55 (2 H, m) and 7.60–7.69 (2 H, m); δ_C(75.5 MHz) 63.5 (q), 105.5 (d), 126.3 (s), 129.2 (d), 129.3 (d), 136.3 (s), 139.4 (s) and 180.4 (s); *m*/*z* (EI): 257 (M$^+$, 60%), 227 (81), 191 (34) and 168 (100); *m*/*z* (CI): 258 (M$^+$ + H, 100%), 228 (51) and 169 (3); HRMS: $C_{10}H_8NOS_2{}^{35}Cl$ requires 256.97357, found 256.97340; $C_9{}^{13}CH_8NOS_2{}^{35}Cl$ requires 257.97693, found 257.97680; $C_{10}H_8NOS_2{}^{37}Cl$ requires 258.97064, found 258.97050.

Synthesis of spiro[4.5]decan-6,10-dione 20 as a reference compound

248 mg (1.06 mmol) of **17c** and 159 mg (1.07 mmol) **6**[18] were dissolved in 30 ml anhydrous acetonitrile. The reaction mixture was evenly distributed between three pyrex reactors, and the dissolved oxygen was removed by ultrasound treatment for 15 min under a steady flow of argon. The solutions were irradiated under argon for 180 min by means of a medium-pressure mercury lamp. After evaporation of the solvent the residue was purified by column chromatography [silica gel, diethyl ether–*n*-pentane (1 : 3)] to yield 24 mg (13%, R_f = 0.12) of **20**; δ_H(300 MHz) 1.67 (4 H, m), 1.98 (2 H, m), 2.06 (4 H, m) and 2.68 (4 H, t, *J* 6.8); δ_C(75.5 MHz) 17.7 (t), 26.4 (t), 33.1 (t), 37.9 (t), 72.5 (s) and 208.8 (s). The remaining analytical data were in accordance with literature values.[16]

Reaction of 6 with $NO_3^•$

57 mg (104 µmol) CAN and 20 mg (133 µmol) **6** were dissolved in anhydrous acetonitrile (10 ml) in a pyrex reactor. The dissolved oxygen was removed by ultrasound treatment for 15 min under a steady flow of argon. The mixture was irradiated under argon until the yellow color had dissappeared (20 min). The solvent was evaporated, the standard (*n*-hexadecane) was added and the residue was diluted with water. The mixture was extracted with diethyl ether, filtrated (silica gel, diethyl ether) and analyzed by GC.

Reaction of 6 with $SO_4^{•-}$

20 mg (135 µmol) **6** were dissolved in 3 ml acetonitrile and mixed with a solution of 80 mg (297 µmol) potassium

peroxodisulfate in 1 ml water. A solution of 129 mg (339 mmol) of ferrous ethylenediammonium sulfate tetrahydrate in 3 ml of water was added dropwise over 5 min. The solution was stirred for 15 min at room temperature, after which the standard (*n*-hexadecane) was added. The mixture was diluted with water, extracted with diethyl ether, filtrated (silica gel, diethyl ether) and analyzed by GC.

Reaction of 6 with $RC(O)O^{\bullet}$, $ROC(O)O^{\bullet}$, $RO^{\bullet}$ and $HO^{\bullet}$

In a typical experiment 34 µmol of **15** or **18** and 103 µmol **6** were dissolved in 10 ml anhydrous acetonitrile in a pyrex reactor. The dissolved oxygen was removed by ultrasound treatment for 15 min under a steady flow of argon. The mixture was irradiated under argon for 60–90 min and analyzed by GC.

Reaction of 6 with 15h–i

The Barton esters **15h**–**k** were unstable[6,30] and could not be isolated. They were prepared *in situ* in analogy to a procedure described by Ollivier and Renaud.[31] In a typical experiment 600 µmol of methyl or phenyl choroformate or ethoxalyl chloride, respectively, and 650 µmol of the sodium salt of *N*-hydroxypyridine-2(1*H*)-thione were dissolved in 3 ml of anhydrous benzene and stirred at room temperature in the dark for 1 hour. 0.2 ml (40 µmol) of this solution were added to a solution of 18 mg (120 µmol) **6** in 10 ml anhydrous acetonitrile in a pyrex reactor. The dissolved oxygen was removed by ultrasound treatment for 15 min under a steady flow of argon. The mixture was irradiated under argon for 60–90 min and analyzed by GC.

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft, Fonds der Chemischen Industrie and the Dr Otto Röhm-Gedächtnisstiftung for financial support.

References

1 U. Wille, *Chem. Eur. J.*, 2002, **8**, 340.
2 (*a*) U. Wille and C. Plath, *Liebigs Ann.*, 1997, 111; (*b*) U. Wille and L. Lietzau, *Tetrahedron*, 1999, **55**, 10119; (*c*) U. Wille and L. Lietzau, *Tetrahedron*, 1999, **55**, 11456; (*d*) L. Lietzau and U. Wille, *Heterocycles*, 2001, **55**, 377.
3 U. Wille, *Org. Lett.*, 2000, **2**, 3485.
4 U. Wille, *Tetrahedron Lett.*, 2002, **43**, 1239.
5 U. Wille, *J. Am. Chem. Soc.*, 2002, **124**, 14.
6 C. Jargstorff and U. Wille, unpublished results.
7 J. Fossey, D. Lefort and J. Sorba, *Free Radicals in Organic Chemistry*, Masson, Paris, 1995.
8 The reversibility of allyloxyl radical formation was considered by: F. E. Ziegler and A. K. Petersen, *J. Org. Chem.*, 1994, **59**, 2707.
9 (*a*) D. Laurie, D. C. Nonhebel, C. J. Suckling and J. C. Walton, *Tetrahedron*, 1993, **49**, 5869; (*b*) V. Krishnamurthy and V. H. Rawal, *J. Org. Chem.*, 1997, **62**, 1572.
10 B. Giese, in *Houben-Weyl, Methoden der Organischen Chemie, Band E 19a C-Radikale*, ed. M. Regitz and B. Giese, Georg Thieme Verlag, Stuttgart, New York, 1989, p. 133.
11 *Handbook of Chemistry and Physics*, ed. R. C. Weast, M. J. Astle and W. H. Beyer, CRC Press, Boca Raton, Florida, 67th edn., 1986.
12 (*a*) E. Baciocchi, T. Del Giacco, C. Rol and G. V. Sebastiani, *Tetrahedron Lett.*, 1985, **26**, 541; (*b*) E. Baciocchi, T. Del Giacco, C. Rol and G. V. Sebastiani, *Tetrahedron Lett.*, 1985, **26**, 3353; (*c*) E. Baciocchi, T. Del Giacco and G. V. Sebastiani, *Tetrahedron Lett.*, 1987, **28**, 1941; (*d*) E. Baciocchi, T. Del Giacco, S. M. Murgia and G. V. Sebastiani, *J. Chem. Soc., Chem. Commun.*, 1987, 1246; (*e*) L. Grossi and S. Strazzari, *J. Org. Chem.*, 1999, **64**, 8076.
13 (*a*) F. Minisci and A. Citterio, *Acc. Chem. Res.*, 1983, **16**, 27; (*b*) C. Walling and D. M. Camaioni, *J. Am. Chem. Soc.*, 1975, **97**, 1603; (*c*) C. Walling, D. M. Camaioni and S. S. Kim, *J. Am. Chem. Soc.*, 1978, **100**, 4814; (*d*) F. Effenberger and H. Kottmann, *Tetrahedron*, 1985, **41**, 4171.
14 D. H. R. Barton and J. A. Ferreira, *Tetrahedron*, 1996, **52**, 9347 and references therein.
15 J. Hartung, *Eur. J. Org. Chem.*, 2001, 619 and references therein.
16 (*a*) J. R. Williams and G. M. Sarkisian, *J. Org. Chem.*, 1974, **39**, 1028; (*b*) H. Hart and L. R. Lerner, *J. Org. Chem.*, 1967, **32**, 2669.
17 H. J. Wüthrich, A. Siewinski and H. Schaffner, *Helv. Chim. Acta*, 1973, **56**, 239.
18 (*a*) M. F. Wempe and J. R. Grunwell, *Tetrahedron Lett.*, 2001, **41**, 6709; (*b*) M. F. Wempe and J. R. Grunwell, *J. Org. Chem.*, 1995, **60**, 2714 and references therein.
19 A reversible addition of a tin-centered radical to the $C\equiv C$ triple bond in **6** was proposed: J. E. Baldwin, R. M. Adlington and J. Robertson, *Tetrahedron*, 1991, **47**, 6795.
20 H. Zipse and M. Bootz, *J. Chem. Soc., Perkin Trans. 2*, 2001, 1566 and references therein.
21 (*a*) N. W. Luft, *Z. Elektrochem.*, 1956, **60**, 94; (*b*) L. Batt and R. D. McCulloch, *Int. J. Chem. Kinet.*, 1976, **8**, 491; (*c*) Y. D. Orlov and Y. A. Lebedev, *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)*, 1984, **33**, 1227.
22 P. Gray and A. Williams, *Trans. Faraday Soc.*, 1959, **55**, 760.
23 (*a*) L. Batt and R. D. McCulloch, *Int. J. Chem. Kinet.*, 1976, **8**, 911; (*b*) J. E. Mihalick, G. G. Gatev and J. I. Brauman, *J. Am. Chem. Soc.*, 1996, **118**, 12424.
24 M. A. Grela and A. J. Colussi, *J. Phys. Chem.*, 1986, **90**, 434.
25 L. Grossi and G. Placucci, *J. Chem. Soc., Chem. Commun.*, 1985, 943.
26 J. T. Niiranen, D. Gutman and L. N. Krasnoperov, *J. Phys. Chem.*, 1992, **96**, 5881.
27 J. L. Holmes, F. P. Lossing and P. M. Mayer, *J. Am. Chem. Soc.*, 1991, **113**, 9723.
28 J. M. Nicovich, C. A. van Dijk, K. D. Kreutter and P. H. Wine, *J. Phys. Chem.*, 1991, **95**, 9890.
29 D. H. R. Barton and C. Tadchdjian, *Tetrahedron*, 1992, **48**, 7109.
30 G. Bucher, M. Halupka, C. Kolano, O. Schade and W. Sander, *Eur. J. Org. Chem.*, 2001, 545 and references therein.
31 C. Ollivier and P. Renaud, *Angew. Chem.*, 2000, **112**, 946; C. Ollivier and P. Renaud, *Angew. Chem., Int. Ed.*, 2000, **39**, 925.