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Structural Effects on the β-Scission Reaction of Tertiary Arylcarbinyloxyl Radicals. The Role of α-Cyclopropyl and α-Cyclobutyl Groups

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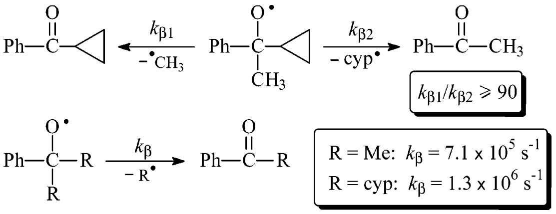
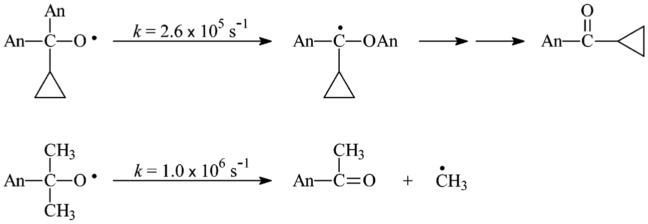


A product and time-resolved kinetic study on the reactivity of tertiary arylcarbinyloxyl radicals bearing α-cyclopropyl and α-cyclobutyl groups has been carried out. Both the 1-cyclopropyl-1-phenylethoxyl (**1$^{\bullet}$**) and α,α-dicyclopropylphenylmethoxyl (**2$^{\bullet}$**) radicals undergo β-scission to give cyclopropyl phenyl ketone as the major or exclusive product with rate constants higher than that measured for the cumyloxyl radical. It is proposed that in the transition state for β-scission of **1$^{\bullet}$** and **2$^{\bullet}$**, formation of the C═O double bond is assisted by overlap with the C−C bonding orbitals of the cyclopropane ring. With tertiary arylcarbinyloxyl radicals bearing α-cyclobutyl groups such as the 1-cyclobutyl-1-phenylethoxyl (**4$^{\bullet}$**) and 1-cyclobutyl-1-phenylpropoxyl (**5$^{\bullet}$**) radicals, the fragmentation regioselectivity is essentially governed by the stability of the radical formed by β-scission. Accordingly, **4$^{\bullet}$** undergoes exclusive C-cyclobutyl bond cleavage to give acetophenone, whereas with **5$^{\bullet}$**, competition between C-cyclobutyl and C-ethyl bond cleavage, leading to propiophenone and cyclobutylphenyl ketone in a 2:1 ratio, is observed.

Recently, while investigating the *O*-neophyl rearrangement of ring-substituted 1,1-diarylalkoxyl radicals, we observed that among the radicals studied the cyclopropyl[bis(4-methoxyphenyl)]methoxyl radical displayed the lowest reactivity, undergoing 1,2-aryl shift with $k = 2.6 \times 10^5$ s^{-1}.[1] No evidence for the formation of products deriving from C-cyclopropyl β-scission but only of the rearrangement product cyclopropyl 4-methoxyphenyl ketone was obtained. Quite interestingly, the rearrangement rate constant measured for this radical is lower than the rate constant measured previously for C-methyl β-scission of the 4-methoxycumyloxyl radical, $k = 1.0 \times 10^6$ s^{-1} (Scheme 1: An = 4-MeOC$_6$H$_4$),[2,3] leading to the suggestion that in alkoxyl radicals C-cyclopropyl β-scission occurs at a significantly lower rate than C-Me β-scission, in line with the slightly higher stability of the methyl radical as compared to the cyclopropyl one (on the basis of the CH$_3$−H and c-C$_3$H$_5$−H BDEs: 105.0 and 106.3 kcal mol^{-1}, respectively).[4,5]

SCHEME 1



C−C β-scission is one of the most important reactions of alkoxyl radicals, and accordingly, this reaction has

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[1] Aureliano Antunes, C. S.; Bietti, M.; Ercolani, G.; Lanzalunga, O.; Salamone, M. *J. Org. Chem.* **2005**, *70*, 3884−3891.

[2] Baciocchi, E.; Bietti, M.; Salamone, M.; Steenken, S. *J. Org. Chem.* **2002**, *67*, 2266−2270.

[3] Unfortunately, it was not possible to study the reactivity of the 1,1-di(4-methoxyphenyl)ethoxyl radical as the instability of the precursor 1,1-di(4-methoxyphenyl)ethanol did not allow the synthesis of the corresponding *tert*-butyl peroxide (see ref 1).

[4] Luo, Y.-R. *Handbook of Bond Dissociation Energies in Organic Compounds;* CRC Press LLC: Boca Raton, FL, 2003.

[5] For a critical discussion on the relative stabilities of alkyl radicals, see refs 6 and 7.

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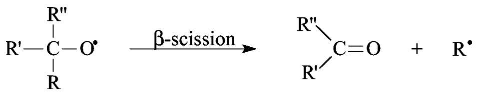
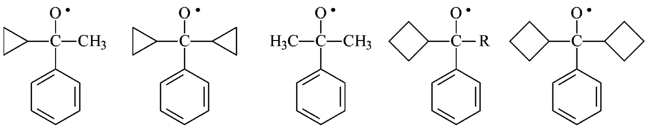
SCHEME 2



been thoroughly investigated[8−16] and has found increasing application in synthetically useful procedures.[17−21] With tertiary alkoxyl radicals bearing different alkyl groups it is possible, at least in principle, to obtain three different C−C bond fragmentations (Scheme 2), and consequently, the intramolecular selectivity in the β-scission reactions of alkoxyl radicals has been the subject of detailed investigation.

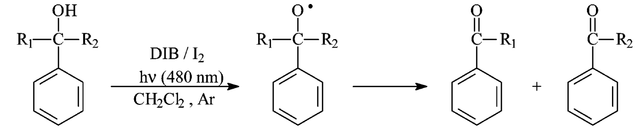
The main conclusion of these studies was that cleavage generally leads to the most stable possible alkyl radical, and it was also shown that other factors such as the stability of the product ketone (in some β-scission reactions leading to the same radical $R^{\bullet}$)[8a,13b] or, when dealing with cycloalkoxyl radicals, the release of ring strain associated to ring opening[13a,c,15,22−24] may play an important role. Along this line, following our continuous interest in the role of structural effects on the β-scission reactions of alkoxyl radicals and taking advantage of the fact that arylcarbinyloxyl radicals display an absorption band in the visible region of the spectrum,[2,25] it seemed particularly interesting to study the reactivity of tertiary arylcarbinyloxyl radicals bearing one or two α-cyclopropyl groups to test whether the presence of these groups influences the reactivity toward β-scission of these radicals. For this purpose, we have carried out a product and time-resolved kinetic study on the reactivity of the 1-cyclopropyl-1-phenylethoxyl and dicyclopropylphenylmethoxyl radicals (**1**$^{\bullet}$ and **2**$^{\bullet}$, respectively) whose structures are shown in Chart 1. The results obtained for these radicals have been compared with those obtained analogously for the cumyloxyl radical (**3**$^{\bullet}$).

CHART 1



1$^{\bullet}$ **2**$^{\bullet}$ **3**$^{\bullet}$ **4**$^{\bullet}$ R = CH_3 **6**$^{\bullet}$
5$^{\bullet}$ R = CH_2CH_3

SCHEME 3



1a: R_1 = Me, R_2 = cyp
2a: R_1 = R_2 = cyp
3a: R_1 = R_2 = Me
4a: R_1 = Me, R_2 = cyb
5a: R_1 = Et, R_2 = cyb
6a: R_1 = R_2 = cyb

The study has been also extended to tertiary arylcarbinyloxyl radicals bearing one or two α-cyclobutyl groups (radicals **4**$^{\bullet}$−**6**$^{\bullet}$ in Chart 1). However, because time-resolved experiments have shown that **4**$^{\bullet}$ displays a reactivity which exceeds the time resolution of the ns laser flash photolysis apparatus employed (see below), with radicals **5**$^{\bullet}$ and **6**$^{\bullet}$, which can be reasonably expected to display a higher reactivity than **4**$^{\bullet}$, only product studies have been carried out.

Results

Product Studies. Arylcarbinyloxyl radicals **1**$^{\bullet}$−**6**$^{\bullet}$ have been generated photochemically by visible light irradiation of CH_2Cl_2 solutions containing the parent arylalkanols (**1a**−**6a**), (diacetoxy)iodobenzene (DIB), and I_2. It is well established that under these conditions the DIB/I_2 reagent converts alcohols into intermediate hypoiodites which are then photolyzed to give alkoxyl radicals,[18,19,22,26] precursors of the observed reaction products. With arylalkanols **1a**−**6a**, the alkoxyl radicals so formed are expected to undergo β-scission to give the corresponding aryl ketones (Scheme 3: cyp = cyclopropyl; cyb = cyclobutyl).

Argon-saturated CH_2Cl_2 solutions containing arylalkanols **1a**−**6a** (10 mM), DIB (22 mM), and I_2 (10 mM) were irradiated with visible light ($\lambda_{\max} \approx 480$ nm) at $T = 20$ °C. The irradiation time was chosen in such a way as

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(6) Coote, M. L.; Pross, A.; Radom, L. *Org. Lett.* **2003**, *5*, 4689−4692.

(7) Matsunaga, N.; Rogers, D. W.; Zavitsas, A. A. *J. Org. Chem.* **2003**, *68*, 3158−3172.

(8) (a) Newcomb, M.; Daublain, P.; Horner, J. H. *J. Org. Chem.* **2002**, *67*, 8669−8671. (b) Horner, J. H.; Choi, S.-Y.; Newcomb, M. *Org. Lett.* **2000**, *2*, 3369−3372.

(9) (a) Nakamura, T.; Watanabe, Y.; Suyama, S.; Tezuka, H. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1364−1369. (b) Nakamura, T.; Busfield, W. K.; Jenkins, I. D.; Rizzardo, E.; Thang, S. H.; Suyama, S. *J. Org. Chem.* **2000**, *65*, 16−23.

(10) Wilsey, S.; Dowd, P.; Houk, K. N. *J. Org. Chem.* **1999**, *64*, 8801−8811.

(11) (a) Avila, D. V.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1993**, *115*, 466−470. (b) Neville, A. G.; Brown, C. E.; Rayner, D. M.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1989**, *111*, 9269−9270.

(12) (a) Banks, J. T.; Scaiano, J. C. *J. Am. Chem. Soc.* **1993**, *115*, 6409−6413. (b) Baignée, A.; Howard, J. A.; Scaiano, J. C.; Stewart, L. C. *J. Am. Chem. Soc.* **1983**, *105*, 6120−6123. (c) Mendenhall, G. D.; Stewart, L. C.; Scaiano, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 5109−5114.

(13) (a) Walling, C.; Clark, R. T. *J. Am. Chem. Soc.* **1974**, *96*, 4530−4533. (b) Walling, C. *Pure Appl. Chem.* **1967**, *15*, 69−80. (c) Walling, C.; Padwa, A. *J. Am. Chem. Soc.* **1963**, *85*, 1593−1597.

(14) (a) Bacha, J. D.; Kochi, J. K. *J. Org. Chem.* **1965**, *30*, 3272−3278. (b) Kochi, J. K. *J. Am. Chem. Soc.* **1962**, *84*, 1193−1197.

(15) Greene, F. D.; Savitz, M. L.; Osterholtz, F. D.; Lau, H. H.; Smith, W. N.; Zanet, P. M. *J. Org. Chem.* **1963**, *28*, 55−64.

(16) Gray, P.; Williams, A. *Chem. Rev.* **1959**, *59*, 239−328.

(17) Yoshimitsu, T.; Sasaki, S.; Arano, Y.; Nagaoka, H. *J. Org. Chem.* **2004**, *69*, 9262−9268.

(18) Boto, A.; Hernández, R.; Montoya, A.; Suárez, E. *Tetrahedron Lett.* **2004**, *45*, 1559−1563. Francisco, C. G.; Gonzalez, C. C.; Paz, N. R.; Suárez, E. *Org. Lett.* **2003**, *5*, 4171−4173. Alonso-Cruz, C. R.; Kennedy, A. R.; Rodriguez, M. S.; Suárez, E. *Org. Lett.* **2003**, *5*, 3729−3732. Suárez, E.; Rodriguez, M. S. In *Radicals in Organic Synthesis*; Renaud, P., Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 2, pp 440−454.

(19) Togo, H.; Katohgi, M. *Synlett.* **2001**, *5*, 565−581.

(20) (a) Zhang, W. In *Radicals in Organic Synthesis*; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, Germany, 2001; Vol. 2, pp 234−245. (b) Dowd, P.; Zhang, W. *Chem. Rev.* **1993**, *93*, 2091−2115.

(21) Yet, L. *Tetrahedron* **1999**, *55*, 9349−9403.

(22) Aureliano Antunes, C. S.; Bietti, M.; Lanzalunga, O.; Salamone, M. *J. Org. Chem.* **2004**, *69*, 5281−5289.

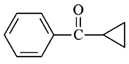
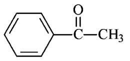
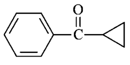
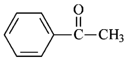
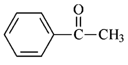
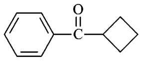
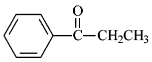
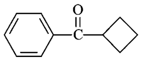
(23) (a) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 2674−2681. (b) Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 230−234.

(24) Bietti, M.; Lanzalunga, O.; Salamone, M. *J. Org. Chem.* **2005**, *70*, 1417−1422.

(25) (a) Avila, D. V.; Ingold, K. U.; Di Nardo, A. A.; Zerbetto, F.; Zgierski, M. Z.; Lusztyk, J. *J. Am. Chem. Soc.* **1995**, *117*, 2711−2718. (b) Avila, D. V.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1992**, *114*, 6576−6577.

(26) Courtneidge, J. L.; Lusztyk, J.; Pagè, D. *Tetrahedron Lett.* **1994**, *35*, 1003−1006.

TABLE 1. Product Distributions and Yields Observed after Irradiation of Argon-Saturated CH_2Cl_2 Solutions Containing Arylalkanols 1a−6a, DIB, and I_2[a]

substrate	products	yield (%)
1a	 	45[b]
2a		24
3a		15
4a		> 99[c] 65[d]
5a	 	51[d,e]
6a		56[d]

[a] [DIB] = 22 mM, [I_2] = 10 mM, [substrate] = 10 mM, irradiation wavelength = 480 nm, irradiation time = 15 min, T = 20 °C. [b] Product yields: cyclopropyl phenyl ketone 45%, acetophenone ≤ 0.5%. [c] Irradiation time = 2 min. Under these conditions, complete conversion of the substrate (**4a**) was observed. [d] Irradiation time = 1 min, using only 4 of the 10 15-W lamps available. [e] Product yields: propiophenone 34%, cyclobutyl phenyl ketone 17%.

to avoid complete substrate conversion. After workup of the reaction mixture, the reaction products were identified by GC (comparison with authentic samples) and GC-MS and were quantitatively determined, together with the unreacted substrate by GC, using bibenzyl as internal standard. The product distributions and yields observed after irradiation of argon-saturated CH_2Cl_2 solutions containing substrates **1a**−**6a**, DIB, and I_2 are collected in Table 1.

The reactions of α,α-dicyclopropylphenylmethanol (**2a**) and 2-phenyl-2-propanol (**3a**) led to the formation of cyclopropyl phenyl ketone and acetophenone, respectively, as the exclusive reaction product. With 1-cyclopropyl-1-phenylethanol (**1a**), formation of cyclopropyl phenyl ketone as the major product, accompanied by traces of acetophenone, was instead observed, and a lower limit for the product ratio cyclopropyl phenyl ketone/acetophenone ≥90 was determined.

The reactions of 1-cyclobutyl-1-phenylethanol (**4a**) and α,α-dicyclobutylphenylmethanol (**6a**) led to the formation of acetophenone and cyclobutyl phenyl ketone, respectively, as the exclusive reaction product. With 1-cyclobutyl-1-phenylpropanol (**5a**), formation of propiophenone and cyclobutyl phenyl ketone in a 2:1 ratio was observed.

Time-Resolved Kinetic Studies. Alkoxyl radicals **1**$^{\bullet}$, **2**$^{\bullet}$, and **4**$^{\bullet}$ have been generated in MeCN by 266-nm laser flash photolysis (LFP) of the parent *tert*-butyl peroxides **1p**, **2p**, and **4p** (equation 1: cyp = cyclopropyl; cyb = cyclobutyl), which in turn have been synthesized by reaction of arylalkanols **1a**, **2a**, and **4a** with *tert*-butyl hydroperoxide in the presence of *p*-toluenesulfonic acid according to a slight modification of a previously described procedure (see Supporting Information).[2,27] To obtain information on the effect of solvent polarity on the β-scission reaction, radicals **1**$^{\bullet}$ and **2**$^{\bullet}$ have been also generated in MeCN/H_2O 1:1 and CF_3CH_2OH.

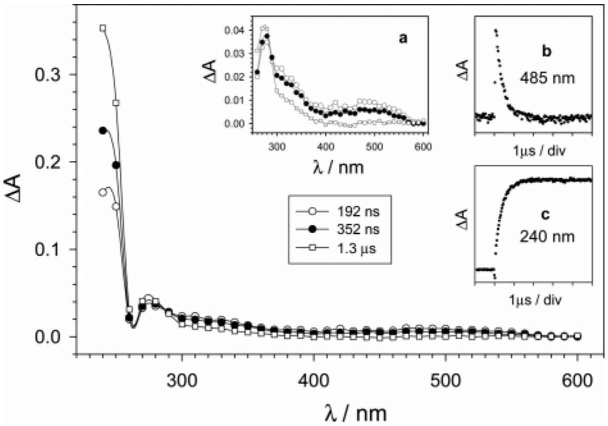
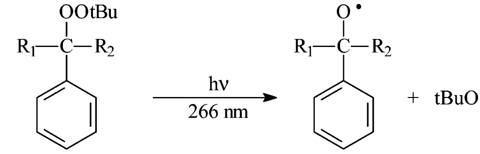


FIGURE 1. Time-resolved absorption spectra observed after 266-nm LFP of **1p** (10.4 mM) in an argon-saturated MeCN solution at 192 ns (empty circles), 352 ns (filled circles), and 1.3 μs (empty squares) after the 8 ns, 10 mJ laser pulse. Insets: (a) Zoom-in of the 260−600 nm region. (b) First-order decay of radical **1**$^{\bullet}$ monitored at 485 nm. (c) Corresponding first-order buildup of absorption at 240 nm, assigned to the product cyclopropyl phenyl ketone.



(1)

1p: R_1 = Me, R_2 = cyp
2p: R_1 = R_2 = cyp
4p: R_1 = Me, R_2 = cyb

The cumyloxyl radical **3**$^{\bullet}$ was instead generated in MeCN and CF_3CH_2OH by 266-nm LFP of dicumyl peroxide (5.0×10^{-3} M) as described previously.[25]

In MeCN, alkoxyl radicals **1**$^{\bullet}$ and **2**$^{\bullet}$ display a broad absorption band in the visible region of the spectrum centered around 485 nm, which is unaffected by oxygen, in line with previous observations on the spectral properties and reactivity toward oxygen of the cumyloxyl radical **3**$^{\bullet}$.[2,11a,25,28] The visible absorption band undergoes a first-order decay, leading in both cases to a corresponding strong increase in absorption in the UV region of the spectrum, assigned, on the basis of the product studies described above, to the product cyclopropyl phenyl ketone formed by β-scission in radicals **1**$^{\bullet}$ and **2**$^{\bullet}$. Quite interestingly, as compared to MeCN, in MeCN/H_2O 1:1 and CF_3CH_2OH, a red-shift in the position of the visible absorption band maximum of radicals **1**$^{\bullet}$−**3**$^{\bullet}$ of ≈30 nm is observed.[2]

As an example, Figure 1 displays the time-resolved absorption spectra observed after LFP of an argon-

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[27] Hendrickson, W. H.; Nguyen, C. C.; Nguyen, J. T.; Simons, K. T. *Tetrahedron Lett.* **1995**, *36*, 7217−7220.

[28] Actually, the time-resolved absorption spectrum of the α,α-dicyclopropylphenylmethoxyl radical (**2**$^{\bullet}$) recorded in MeCN (see Figure S1 in the Supporting Information) shows a very broad absorption band extending from approximately 550 nm down to the UV region, characterized by maxima at ≈490, 420, and 360 nm.

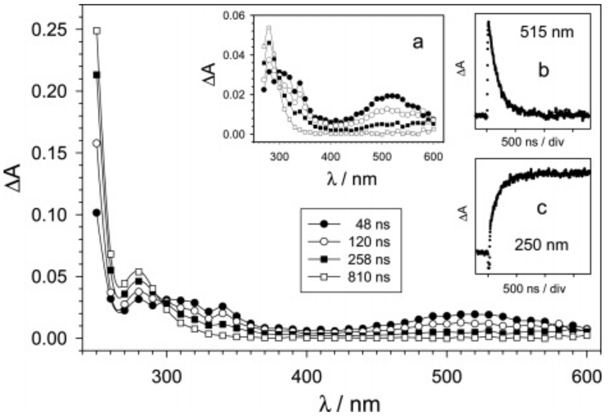

FIGURE 2. Time-resolved absorption spectra observed after 266-nm LFP of dicumyl peroxide (5.0 mM) in an argon-saturated CF_3CH_2OH solution at 48 (filled circles), 120 (empty circles), 258 (filled squares), and 810 ns (empty squares) after the 8 ns, 10 mJ laser pulse. Insets: (a) Zoom-in of the 260–600 nm region. (b) First-order decay of radical $\mathbf{3}^{\bullet}$ monitored at 515 nm. (c) Corresponding first-order buildup of absorption at 250 nm, assigned to the product acetophenone.

saturated MeCN solution containing peroxide **1p**, showing after 192 ns (empty circles) a broad absorption band centered at 485 nm, which is assigned to the radical $\mathbf{1}^{\bullet}$. This species undergoes a first-order decay (inset b) accompanied by a corresponding buildup of optical density at 240 nm (inset c) assigned to cyclopropyl phenyl ketone (an isosbestic point is visible at 290 nm) which, accordingly, is characterized by an absorption maximum at this wavelength. As expected, both the 485-nm and the 240-nm bands were not affected by the presence of oxygen. Also visible is a relatively stable absorption band centered at 280 nm which, on the basis of the comparison with literature data,[2,29] is assigned to the *tert*-butoxyl radical, formed according to eq 1.[30]

The time-resolved absorption spectra observed after LFP of an argon-saturated MeCN solution containing peroxide **2p** are instead displayed in Figure S1 (see Supporting Information).

Figure 2 displays the time-resolved absorption spectra observed after LFP of an argon-saturated CF_3CH_2OH solution containing dicumyl peroxide. The spectrum recorded after 48 ns is characterized by a broad absorption band in the visible region centered at 515 nm and by a band in the UV region between 300 and 350 nm, which are assigned to the cumyloxyl radical $\mathbf{3}^{\bullet}$.[2,25] As compared to the spectrum of $\mathbf{3}^{\bullet}$ recorded in MeCN,[2,25] a 30-nm red-shift in the position of the visible absorption band maximum is observed (see later). This species undergoes a first-order decay (inset b) accompanied by a corresponding buildup of optical density at 250 nm (inset c) and 280 nm assigned to acetophenone (an isosbestic point is visible at 300 nm).

TABLE 2. Visible Absorption Band Maximum Wavelengths, Decay, and Buildup Rate Constants for Alkoxyl Radicals ($\mathbf{1}^{\bullet}$–$\mathbf{4}^{\bullet}$) Measured at T = 25 °C

radical	conditions		λ_{max}/nm[a]	$k_{\downarrow}$/s^{-1} [b]	$k_{\uparrow}$/s^{-1} [c]
$\mathbf{1}^{\bullet}$	MeCN	Ar	485	3.0×10^6	3.2×10^6
	MeCN	O_2	485	3.1×10^6	3.0×10^6
	MeCN/H_2O[d]	Ar	515	9.3×10^6	8.9×10^6
	CF_3CH_2OH	Ar	515	2.1×10^7	2.2×10^7
$\mathbf{2}^{\bullet}$	MeCN	Ar	490[e]	1.3×10^6	1.3×10^6
	MeCN	O_2	490[e]	1.1×10^6	1.4×10^6
	MeCN/H_2O[d]	Ar	[f]	4.6×10^6	4.5×10^6
	CF_3CH_2OH	Ar	[f]	1.6×10^7	[g]
$\mathbf{3}^{\bullet}$	MeCN	Ar	485	7.1×10^5	
	CF_3CH_2OH	Ar	515	6.1×10^6	
$\mathbf{4}^{\bullet}$	MeCN	Ar			$\geq 8 \times 10^7$ [h]

[a] Visible absorption band maximum of the alkoxyl radical. [b] Measured following the decay of the alkoxyl radical at the visible absorption band maximum. [c] Measured following the buildup of the product aryl ketone at 240 or 250 nm. [d] MeCN/H_2O 1:1 (v/v). [e] See ref 28 and Figure S1 in the Supporting Information. [f] λ_{max} between 480 and 530 nm. The low intensity of the visible absorption band did not allow a precise determination of the band maximum under these conditions. [g] A fast buildup was observed, but because of an initial bleaching in the kinetic traces, it was not possible to measure the buildup rate constant. [h] Measured at $T = -10$ °C. Under these conditions, the radical was too reactive to be studied by ns LFP and, on the basis of the buildup at 250 nm, only a lower limit could be determined.

With peroxide **4p**, the time-resolved absorption spectrum observed after LFP of an argon-saturated MeCN solution did not show an absorption band in the visible region, but only the formation, immediately after the laser pulse, of a stable species absorbing around 250 nm assigned on the basis of the results of product studies described above to acetophenone formed after C-cyclobutyl β-scission in $\mathbf{4}^{\bullet}$.

The reactivity of alkoxyl radicals $\mathbf{1}^{\bullet}$ and $\mathbf{2}^{\bullet}$ was measured spectrophotometrically by monitoring the decrease in optical density at their visible absorption maxima and the corresponding buildup in the UV region because of the formation of cyclopropyl phenyl ketone, which were found to follow in all cases first-order kinetics. The corresponding rate constants thus obtained are reported in Table 2. Radical $\mathbf{4}^{\bullet}$ was instead too reactive to be studied by ns LFP and, on the basis of the buildup of the product acetophenone at 250 nm described above, even at $T = -10$ °C only a lower limit for its reactivity could be determined ($k \geq 8 \times 10^7$ s^{-1}).

In the same table, the decay rate constants for the cumyloxyl radical $\mathbf{3}^{\bullet}$ measured at 485 and 515 nm in MeCN and CF_3CH_2OH, respectively, are also included.

Discussion

The results of product studies collected in Table 1 show that the reaction of 1-cyclopropyl-1-phenylethanol (**1a**) leads to the formation of cyclopropyl phenyl ketone and acetophenone in a ≥90 ratio. This result clearly indicates that in $\mathbf{1}^{\bullet}$ cleavage of the C-methyl bond is strongly favored over that of the C-cyclopropyl one, as expected on the basis of the higher stability of the methyl radical as compared to the cyclopropyl one discussed above.[4,5] However, since the difference in BDE between CH_3–H and c-C_3H_5–H has been reported to be around 1 kcal mol^{-1},[4] the large product ratio observed in the reaction of **1a** suggests that the stability of the radical formed after β-scission is not the only factor which governs the fragmentation regioselectivity in $\mathbf{1}^{\bullet}$.

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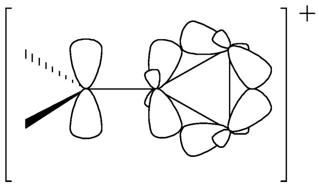
(29) Tsentalovich, Y. P.; Kulik, L. V.; Gritsan, N. P.; Yurkovskaya, A. V. *J. Phys. Chem. A* **1998**, *102*, 7975–7980.

(30) The slight increase in absorption observed at 280 nm is attributed to the formation of cyclopropyl phenyl ketone, which, in addition to the 240-nm band described above, is also characterized by a weak absorption band centered at 276 nm.

Quite surprisingly, the results collected in Table 2 show that as compared to **3**$^\bullet$, an increase in the rate of β-scission is observed with both **1**$^\bullet$ and **2**$^\bullet$. In particular, taking into account the results of product studies, it appears that both C-methyl bond cleavage in **1**$^\bullet$ and C-cyclopropyl bond cleavage in **2**$^\bullet$ occur faster than C-methyl bond cleavage in **3**$^\bullet$, whereas C-cyclopropyl bond cleavage is significantly slower in **1**$^\bullet$ than in **2**$^\bullet$. These observations clearly indicate that the presence of an α-cyclopropyl group plays an important role in the alkoxyl radical fragmentation reaction.

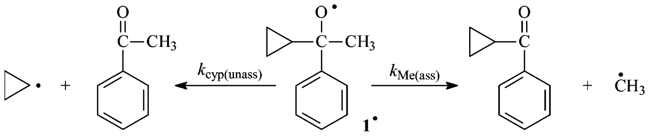
In this context, it is well-known that cyclopropyl substituents strongly stabilize carbocations by interaction of the cyclopropyl C−C bonding orbitals with the vacant p orbital of the carbocation.[31] These orbitals, because of angle strain, have an abnormal amount of p character, and thus when the cyclopropyl group adopts a bisected conformation (with respect to the nodal plane of the vacant p orbital),[32] effective overlap may occur. Accordingly, the efficacy of cyclopropane as a neighboring group in solvolytic reactions is well documented.[34]



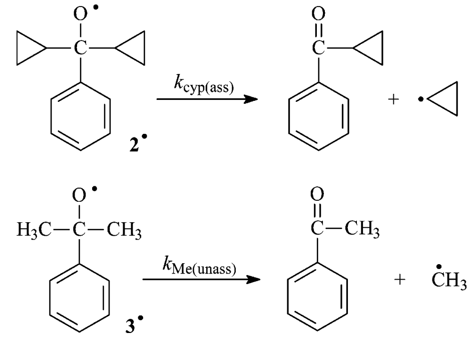
Along this line, it is reasonable to propose that in the transition state for C-methyl β-scission of **1**$^\bullet$ and C-cyclopropyl β-scission of **2**$^\bullet$, formation of the C=O double bond is assisted by overlap with the C−C bonding orbitals of the cyclopropane ring. An analogous assistance is clearly not possible for C-cyclopropyl β-scission in **1**$^\bullet$ and for C-methyl β-scission in the cumyloxyl radical **3**$^\bullet$.

Quite importantly, cyclopropyl participation involving overlap between the C−C bonding orbitals of the cyclopropane ring and developing p orbitals has been also proposed in other reactions, such as for example, the thermolysis of azo compounds[35] and the decarbonylation of tricyclic alkenones.[36,37]

SCHEME 4



SCHEME 5



By combining the product ratio determined for the reaction of **1a** (Table 1) with the decay rate constant measured for **1**$^\bullet$ (Table 2), the partial rate constants for C-methyl bond cleavage *assisted* by the presence of an adjacent cyclopropyl group ($k_{\text{Me(ass)}} = 3.1 \times 10^6$ s^{-1}) and for *unassisted* C-cyclopropyl bond cleavage ($k_{\text{cyp(unass)}} = \leq 3.4 \times 10^4$ s^{-1}) can be derived (Scheme 4).[39,40]

The rate constants measured for **2**$^\bullet$ and **3**$^\bullet$ (Table 2), corrected for the statistical factor, provide instead the assisted rate constant for C-cyclopropyl bond cleavage ($k_{\text{cyp(ass)}} = 6.5 \times 10^5$ s^{-1}) and the unassisted rate constant for C-methyl bond cleavage ($k_{\text{Me(unass)}}$ 3.6×10^5 s^{-1}), respectively (Scheme 5).

Since C-methyl cleavage in **1**$^\bullet$ and C-cyclopropyl cleavage in **2**$^\bullet$, as well as C-cyclopropyl cleavage in **1**$^\bullet$ and C-methyl cleavage in **3**$^\bullet$, lead to the formation of the same ketone (cyclopropyl phenyl ketone and acetophenone, respectively), comparison between the pertinent rate constants provides the kinetic effect of the stability of the alkyl radical on the β-scission reaction.

In both the assisted and unassisted reaction, C-methyl cleavage is favored over C-cyclopropyl cleavage, in line with the slightly higher stability of the methyl radical as compared to the cyclopropyl one.[4,5] However, the reactivity ratio decreases on going from the unassisted ($k_{\text{Me(unass)}}/k_{\text{cyp(unass)}} = \geq 10.6$) to the assisted reaction ($k_{\text{Me(ass)}}/k_{\text{cyp(ass)}} = 4.8$), clearly indicating that, as compared to the methyl radical, formation of the cyclopropyl radical benefits to a greater extent from cyclopropyl assistance. The same conclusion arises from the comparison between the assisted and unassisted β-scission reactions leading

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(31) See, for example: Olah, G. A.; Prakash Reddy, V.; Surya Prakash, G. K. *Chem. Rev.* **1992**, *92*, 69−95 and references therein.

(32) The preference for the bisected conformation over the perpendicular one in cyclopropyl substituted cations has been confirmed in several studies (see, for example, ref 33).

(33) Childs, R. F.; Faggiani, R.; Lock, C. J. L.; Mahendran, M.; Zweep, S. D. *J. Am. Chem. Soc.* **1986**, *108*, 1692−1693. Buss, V.; Gleiter, R.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 3927−3933. Baldwin, J. E.; Fogelsong, W. D. *J. Am. Chem. Soc.* **1968**, *90*, 4303−4310.

(34) See, for example: Roberts, D. D. *J. Org. Chem.* **1999**, *64*, 1341−1343. Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry,* 3rd ed.; Harper & Row: New York, 1987, and references therein.

(35) Schmidt, H.; Schweig, A.; Trost, B. M.; Neubold, H. B.; Scudder, P. H. *J. Am. Chem. Soc.* **1974**, *96*, 622−624. Allred, E. L.; Voorhees, K. J. *J. Am. Chem. Soc.* **1973**, *95*, 620−621. Allred, E. L.; Johnson, A. L. *J. Am. Chem. Soc.* **1971**, *93*, 1300−1301.

(36) Battiste, M. A.; Visnick, M. *Tetrahedron Lett.* **1978**, *19*, 4771−4774. Halton, B.; Battiste, M. A.; Rehberg, R.; Deyrup, C. L.; Brennan, M. E. *J. Am. Chem. Soc.* **1967**, *89*, 5964−5965.

(37) Cyclopropyl participation has been also proposed in the ring-opening of tricyclic cyclopropyl ketones, rationalized in terms of the overlap between the scissile cyclopropane C−C bond and the adjacent p orbital (see ref 38).

(38) Monti, S. A. *J. Org. Chem.* **1970**, *35*, 380−383. Monti, S. A.; Bucheck, D. J.; Shepard, J. C. *J. Org. Chem.* **1969**, *34*, 3080−3084.

(39) The product ratio for **1a** has been determined in CH_2Cl_2, while the decay rate constant for **1**$^\bullet$ has been measured in MeCN. In this respect, no significant difference in product ratio should be observed on going from CH_2Cl_2 to MeCN as the solvent is expected to behave in the same way on the two competing fragmentation reactions of the alkoxyl radical.

(40) The decay rate constants for radicals **1**$^\bullet$−**3**$^\bullet$ have been also measured in CH_2Cl_2 as 3.3×10^6, 1.4×10^6, and 1.3×10^6 s^{-1}, respectively; values which are slightly higher than the corresponding ones measured in the more polar solvent MeCN (see Table 2). However, as the rate constants for β-scission of alkoxyl radicals are known to decrease by decreasing solvent polarity (see, for example, refs 2, 11a, and 29), the observation of an increase in rate on going from MeCN to CH_2Cl_2 can be rationalized in terms of the contribution to the decay rate constant of a hydrogen abstraction reaction from the solvent CH_2Cl_2.

to the same radical, where, neglecting differences in stability between the product ketones, cyclopropyl assistance is relatively more important in C-cyclopropyl than in C-methyl cleavage ($k_{\mathrm{cyp(ass)}}/k_{\mathrm{cyp(unass)}} = \geq 19.1$ and ($k_{\mathrm{Me(ass)}}/k_{\mathrm{Me(unass)}} = 8.6$).

As observed previously for the cumyloxyl radical $\mathbf{3}^\bullet$,[2,11a] also the rate constants for β-scission of radicals $\mathbf{1}^\bullet$ and $\mathbf{2}^\bullet$ increase by increasing solvent polarity. Solvent effects on the rate constant for β-scission of the cumyloxyl radical have been studied in detail,[11a] and the increase in rate observed with increasing solvent polarity has been interpreted in terms of the stabilization of the transition state for β-scission through increased solvation of the incipient carbonyl product. Quite interestingly, a fairly good correlation between log k_β and the Dimroth-Reichardt E_T^N parameter has been reported for the β-scission reactions of the cumyloxyl radical $\mathbf{3}^\bullet$ in several solvents.[11a] In this context, also the k_β value measured for $\mathbf{3}^\bullet$ in CF_3CH_2OH (characterized by $E_T^N = 0.898$)[41] fits very well into the log k_β versus E_T^N correlation.[42]

Going from MeCN to MeCN/H_2O 1:1 and CF_3CH_2OH results in a red-shift in $\lambda_{\max}$ (vis) of approximately 30 nm for radicals $\mathbf{1}^\bullet$−$\mathbf{3}^\bullet$.[2] The observation of this effect in H_2O and CF_3CH_2OH but not in other protic solvents such as AcOH, *t*BuOH, and dipolar aprotic ones such as MeCN requires some comment. On the basis of Abraham's α_2^H parameters,[43] CF_3CH_2OH and AcOH are characterized by similar hydrogen bond acidities ($\alpha_2^H = 0.567$ and 0.550, respectively), values that are significantly higher than that determined for H_2O ($\alpha_2^H = 0.353$). Clearly, this solvent property alone cannot be invoked to explain the observed solvent effect on $\lambda_{\max}$ (vis). On the other hand, both H_2O and CF_3CH_2OH are characterized by E_T^N values that are significantly higher than those measured for MeCN, *t*BuOH, and AcOH,[44] suggesting that the combination of different solute/solvent interaction forces (well represented by this empirical parameter) contributes to this effect.[45]

The reactions of 1-cyclobutyl-1-phenylethanol (**4a**) and α,α-dicyclobutylphenylmethanol (**6a**) led to the formation of acetophenone and cyclobutyl phenyl ketone, respectively, as the exclusive reaction product. With 1-cyclobutyl-1-phenylpropanol (**5a**), formation of propiophenone and cyclobutyl phenyl ketone in a 2:1 ratio was instead observed. Clearly in $\mathbf{4}^\bullet$, cleavage of the C-cyclobutyl bond is strongly favored over that of the C-methyl one, as expected on the basis of the large difference in stability between the cyclobutyl and the methyl radical (on the basis of the c-C_4H_7−H and CH_3−H BDEs: 96.8 and 105.0 kcal mol^{-1}, respectively).[4] Differences in radical stability can also be invoked to explain the fragmentation regioselectivity observed with $\mathbf{5}^\bullet$, as the c-C_4H_7−H BDE is reported to be lower than the CH_3CH_2−H one (96.8 and 100.5 kcal mol^{-1}, respectively).[4] An observation that is also supported by kinetic data where, however, even though the high reactivity of $\mathbf{4}^\bullet$ did not allow the determination of its fragmentation rate constant but only of a lower limit ($k_\beta \geq 8 \times 10^7$ s^{-1} at $T = -10$ °C, see Table 2), the comparison of this limit with the rate constant measured for C-ethyl β-scission in the 2-(4-methylphenyl)-2-butoxyl radical ($k_\beta = 1.1 \times 10^7$ s^{-1} at $T = -15$ °C)[24] indicates that in tertiary arylcarbinyloxyl radicals cleavage of the C-cyclobutyl bond is favored over that of the C-ethyl one.

In conclusion, by means of product and time-resolved kinetic studies, convincing evidence has been provided for cyclopropyl participation in the β-scission reactions of tertiary arylcarbinyloxyl radicals bearing α-cyclopropyl groups. It is proposed that β-scission proceeds through a transition state where formation of the C═O double bond is assisted by overlap with the C−C bonding orbitals of the cyclopropane ring. The kinetic data clearly show that both C-methyl and C-cyclopropyl bond cleavage are significantly accelerated by cyclopropyl assistance which, moreover, is relatively more important in the latter than in the former β-scission reaction. In particular, C-cyclopropyl bond cleavage, which is expected to be a relatively slow reaction, when assisted by the presence of an additonal cyclopropyl group becomes faster than C-methyl cleavage in the cumyloxyl radical. With tertiary arylcarbinyloxyl radicals bearing α-cyclobutyl groups, the fragmentation regioselectivity is essentially governed by the stability of the radical formed by β-scission, with cleavage of the C-cyclobutyl bond being favored over that of the C-ethyl one and being the exclusive fragmentation pathway when in competition with C-methyl bond cleavage.

Experimental Section

Materials. Spectroscopic grade MeCN and CF_3CH_2OH were used as received. CH_2Cl_2 was purified prior to use by column chromatography over basic alumina. (Diacetoxy)iodobenzene (DIB), iodine, α,α-dicyclopropylphenylmethanol (**2a**), and 2-phenylpropan-2-ol (**3a**) were of the highest commercial quality available and were used as received. Dicumyl peroxide was recrystallized twice from methanol.

Details of the synthesis of arylalkanols **1a**, **4a**−**6a**, and of the *tert*-butyl arylalkyl peroxides (**1p**, **2p**, and **4p**) are given in the Supporting Information. The purity of the arylalkanols (**1a**−**6a**) employed in the product studies was always ≥99%.

Product Analysis. All the reactions were carried out under an argon atmosphere. Irradiations were performed with visible light (4−10 × 15 W lamps with emission between 400 and 550 nm, $\lambda_{\max} \approx 480$ nm). The reactor was a cylindrical flask equipped with a water cooling jacket thermostated at $T = 20$ °C. Irradiation times were chosen in such a way as to avoid complete substrate consumption. In a typical experiment, a solution of the alcohol (10 mM) in CH_2Cl_2 (5 mL) containing (diacetoxy)iodobenzene (22 mM) and iodine (10 mM) was irradiated for times ranging between 1 and 15 min under Ar bubbling. The reaction mixture was then poured into water and extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with a 10% aqueous thiosulfate solution (2 × 30 mL) and water (2 × 30 mL) and were dried over

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(41) Reichardt, C. *Solvents and Solvent Effects in Organic Chemistry*, 3rd ed.; Wiley-VCH: Weinheim, Germany, 2003.

(42) As it has been pointed out that the E_T^N parameter is mainly related to the solvent anion solvating ability (see ref 41, pp 462−463), the observation of a log k_β versus E_T^N correlation reasonably reflects the development of negative charge on the oxygen atom of the forming carbonyl compound. We thank a referee for this suggestion.

(43) Abraham, M. H.; Grellier, P. L.; Prior, D. V.; Duce, P. P.; Morris, J. J.; Taylor, P. J. *J. Chem. Soc., Perkin Trans. 2* **1989**, 699−711.

(44) $(CH_3)_3COH$, MeCN, AcOH, CF_3CH_2OH, and H_2O are characterized by the following E_T^N values: 0.389, 0.460, 0.648, 0.898, and 1.000, respectively (see ref 41).

(45) In this connection, it is important to point out that in water the red-shift in the cumyloxyl radical $\lambda_{\max}$ (vis) is expected to be significantly greater than 30 nm. See, for example, ref 46 for a discussion on the effect of water on the 4-methoxycumyloxyl radical $\lambda_{\max}$ (vis).

(46) Baciocchi, E.; Bietti, M.; Lanzalunga, O.; Steenken, S. *J. Am. Chem. Soc.* **1998**, *120*, 11516−11517.

anhydrous sodium sulfate. Reaction products were identified by GC (comparison with authentic samples) and GC-MS and were quantitatively determined by GC using bibenzyl as internal standard. Excellent mass balances (≥95%) were obtained in all experiments. Blank experiments performed in the absence of irradiation, keeping the solution in the dark, showed the formation of negligible amounts of reaction products.

Laser Flash Photolysis Studies. Laser flash photolysis experiments were carried out with a laser kinetic spectrometer using the fourth harmonic (266 nm) of a Q-switched Nd:YAG laser. The laser energy was adjusted to ≤10 mJ/pulse by the use of the appropriate filter. A 3-mL Suprasil quartz cell (10 mm × 10 mm) was used for all experiments. Argon- or oxygen-saturated MeCN, MeCN/H_2O 1:1 (v/v), or CF_3CH_2OH solutions of peroxides **1p**, **2p**, and dicumyl peroxide (between 5.0×10^{-3} and 1.0×10^{-2} M, $A_{266} \approx 1.0$) were used. All the experiments were carried out at $T = 25 \pm 0.5$ °C under magnetic stirring. LFP of peroxide **4p** (1.0×10^{-2} M) was instead carried out in argon-saturated MeCN solution at $T = -10$ °C. Rate constants were obtained by averaging four to eight values each consisting of the average of at least three laser shots and were reproducible to within 10%.

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Supporting Information Available: Details on the synthesis and characterization of the precursor arylalkanols and *tert*-butyl arylalkyl peroxides. Time-resolved absorption spectra observed after LFP of peroxide **2p**. This material is available free of charge via the Internet at http://pubs.acs.org.

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