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Reversible Photooxygenation of Alkynylanthracenes: Chemical Generation of Singlet Oxygen under Very Mild Conditions

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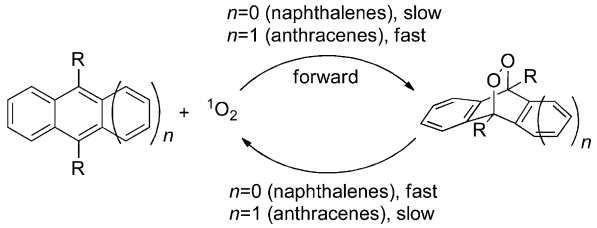
Dedicated to Professor Erich Kleinpeter on the occasion of his 65th birthday

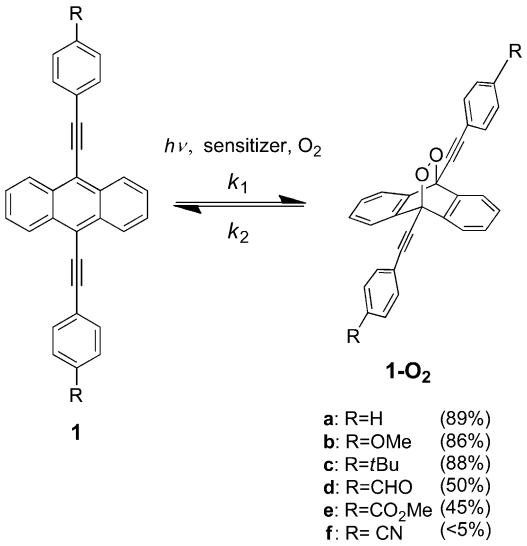
The oxidation of organic compounds with singlet oxygen ($^1O_2$) is important in stereoselective synthesis,[1] medicine,[2] industrial processes[3] and material sciences.[4] Under the conditions used for conventional light-induced photooxygenation, electron transfer from excited states might compete and result in undesired side reactions.[5] Therefore, "dark" oxygenations by chemical sources of $^1O_2$ offer an attractive alternative, especially in biological systems[6] or when precise control over the amount of the donor is required.[7] The reaction of H_2O_2 with hypohalides, lanthanides, or transition metals is a powerful method to produce $^1O_2$ in high quantities but typically requires biphasic or emulsion conditions.[8] In contrast, thermal generation of $^1O_2$ from endoperoxides (EPOs) of acenes can be conducted in organic media. The most important substrates in this field are 1,4-dimethylnaphthalene (DMN)[9] and 9,10-diphenylanthracene (DPA).[10] However, a drawback of their application as $^1O_2$ carriers is that a strong donor is slowly formed from the acene, whereas EPOs that are generated more quickly are too stable to act as $^1O_2$ sources. The formation and the fate of the EPO are both linked to the number of fused rings; whereas naphthalenes react slowly to form the corresponding EPO and favor a rapid reconversion by release of $^1O_2$, anthracenes react faster to form an EPO but their dissociation only starts at high temperatures at which reconversion competes with decomposition (Scheme 1).[11]

Recently, we found that remote substituents of 9,10-arylanthracenes affected the reactivity of EPO formation and cycloreversion, but not in opposite directions as expected.[12] This finding prompted us to incorporate substituents at the bridgehead positions to hopefully give access to new and efficient chemical sources of singlet oxygen.

Herein, we describe the first photooxygenation of alkynyl-substituted anthracenes **1** to give EPOs that release $^1O_2$ in high yield under very mild conditions (Scheme 2). Because the majority of common chemical sources of $^1O_2$ (e.g., EPOs of naphthalenes, arylanthracenes, or heterocyclic compounds) operate at higher temperatures,[13] our new class of acenes is important for applications at low temperatures. Additionally, kinetic results point at different mechanisms of forward and reverse reactions.



Scheme 1. Generation of EPOs from acenes and release of $^1O_2$.



Scheme 2. Reversible photooxygenation of alkynylanthracenes **1**.

Alkynylanthracenes **1a–c** were prepared by Sonogashira coupling of commercially available aryl acetylenes and 9,10-dibromoanthracene,[14] whereas derivatives **1d–f** were synthesized by coupling of aryl bromides and bis-9,10-(trimethylsilylethynyl)anthracene.[15,16] EPOs **1-O$_2$** were obtained by photooxygenation under standard conditions.[16] Although compounds **1a–c** were consumed quantitatively within a few hours, derivatives **1e–f** required longer irradia-

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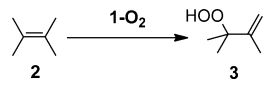
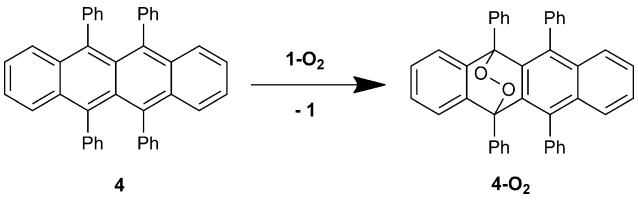
tion times and starting material still remained in the solutions after irradiation for 1 day. EPOs **1-O$_2$** could be isolated by chromatography at −20 °C in moderate to good yields, and were stored in a freezer for several days. The structures of 9,10-EPOs were confirmed by ^{1}H and ^{13}C NMR spectroscopy and mass spectroscopy.[16]

To our surprise, we found that the parent species rapidly regenerated with no formation of rearrangement products if the EPOs were left at room temperature. It is worth noting that the reversible binding of $^1O_2$ to anthracenes has only been reported for substrates with aryl substitution at the 9,10-position. Anthracenes that have hydrogen atoms or alkyl groups do not reversibly bind oxygen and their EPOs decompose on warming.[17] Furthermore, a noticeable reconversion of 9,10-aryl substituted EPOs requires temperatures >80 °C.[18] To the best of our knowledge, the reaction of singlet oxygen with anthracenes functionalized with triple bonds is hitherto unknown. To verify the formation of $^1O_2$ upon cleavage of EPOs **1-O$_2$**, trapping experiments were carried out. When the EPOs were left for 24 h in the dark at room temperature and in the presence of the $^1O_2$ acceptor 2,3-dimethyl-2-butene (**2**; ratio EPO/**2** 1:4), the $^1O_2$–ene reaction product was identified (hydroperoxide **3**; Scheme 3).



Scheme 3. Trapping of $^1O_2$ released by singlet-oxygen donors **1-O$_2$**.

To quantify the fraction of released singlet-state oxygen, we chose rubrene (**4**) as an acceptor because the disappearance of **4** can be measured quantitatively by UV/Vis spectroscopy (Scheme 4, Table 1). Importantly, these experiments were carried out at room temperature. However, physical quenching of $^1O_2$ by the substrate plays a more significant role at room temperature, causing a loss of released $^1O_2$.[19] Therefore, we used DMN-O$_2$ as a reference that can produce $^1O_2$ nearly quantitatively at 40 °C.[18] At room temperature, the production of $^1O_2$ by EPOs of **1a–e** is in the range of 50 %, which is comparable to the measured $^1O_2$ production of the EPO of DMN (Table 1).



Scheme 4. Reaction of rubrene with $^1O_2$ released by endoperoxides **1-O$_2$**.

The half-life ($t_{1/2}$) values for the reconversion of EPOs **1-O$_2$** to the parent form by the release of oxygen were determined from the reappearance of the starting material by UV/Vis spectroscopy (Table 1). The most striking feature of these compounds is revealed by comparison of the rate of reconversion with that of other EPOs; the values are much lower than for all anthracene and naphthalene derivatives found in the literature,[18] even for unsubstituted naphthalene.[20] This exceptional feature provides ideal conditions for the use of alkynylanthracene EPOs as $^1O_2$ donors.[21]

Table 1. Singlet oxygen production measured by the disappearance of rubrene (EPO/rubrene 1:4) and half-life values for reconversion of EPOs **1-O$_2$** at 25 °C.

	Yield of $^1O_2$ [%]	$t_{1/2}$ EPO [min]
1a-O$_2$	57 ± 5	23
1b-O$_2$	53 ± 5	31
1c-O$_2$	67 ± 6	33
1d-O$_2$	48 ± 5	15
1e-O$_2$	43 ± 4	18
DMN-O$_2$	49 ± 5	350
DPA-O$_2$	30–35[a]	600 (at 86 °C)[a]

[a] Measured at elevated temperatures, see ref. [18].

For the evaluation of time profiles of $^1O_2$ generation, donor **1b-O$_2$** was added to solutions of rubrene as the acceptor (**1b-O$_2$**/rubrene 40:1 and 130:1) at room temperature (Figure 1). For comparison with a common $^1O_2$ donor, an analogous experiment was carried out with identical amounts of DMN-O$_2$ (same ratios). At lower concentrations of rubrene (130:1), the rapid release of $^1O_2$ by **1b-O$_2$** caused complete consumption of rubrene within the first few minutes, whereas the reaction with DMN-O$_2$ required around 8 h. At higher rubrene concentrations, the reaction stopped after about 1 h after the addition of **1b-O$_2$**, whereas it continued with DMN-O$_2$. In consequence, EPOs of alkynylanthracenes are superior for short exposure times, for example, in sensitive biological systems[22] and if the acceptor reacts fast.[23]

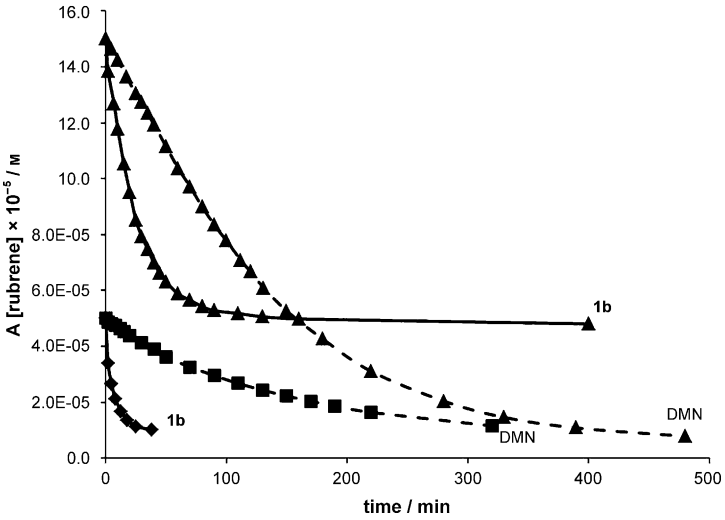


Figure 1. Consumption of rubrene (5×10 (■) and 1.5×10^{-5} M (▲) in $CHCl_3$) measured by the extinction at $\lambda = 530$ nm upon addition of 2×10^{-3} M **1b-O$_2$** (——) and DMN-O$_2$ (-----) in $CHCl_3$.

Encouraged by these findings, we turned our attention towards the reactivity of the forward reaction to evaluate the suitability of alkynylanthracenes **1** as carriers of $^1O_2$. Time

profiles for the disappearance of alkynylanthracenes **1**, anthracene (ANT), DPA, and DMN upon photooxygenation were recorded under identical conditions (Figure 2).[16]

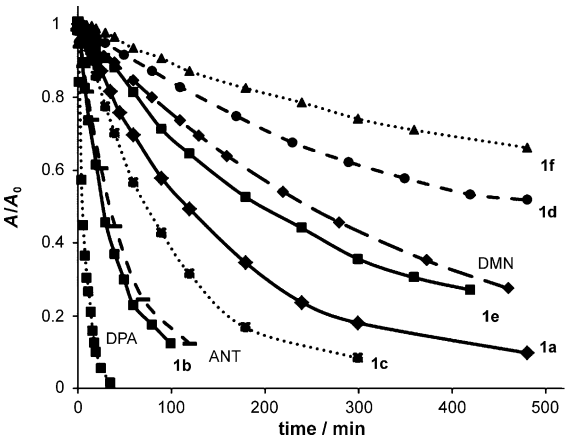


Figure 2. Absorbance vs. time profiles of λ_{max} for alkynylanthracenes **1a**–**f**, ANT, DPA, and DMN under continuous irradiation in the presence of the sensitizer tetraphenylporphyrin (TPP).

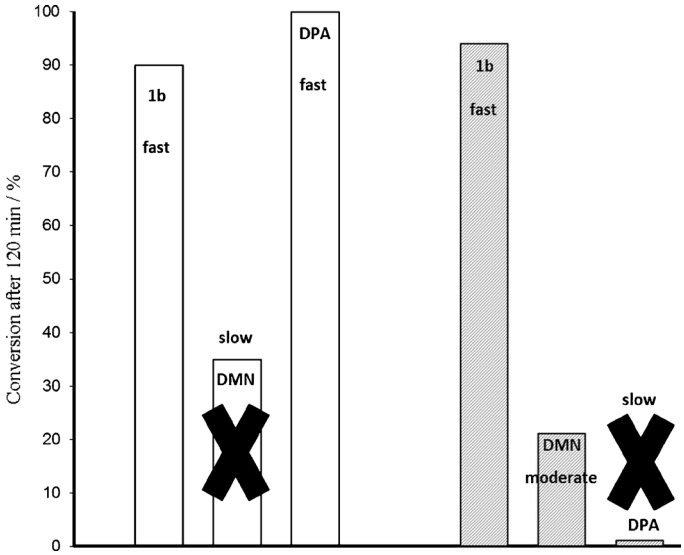
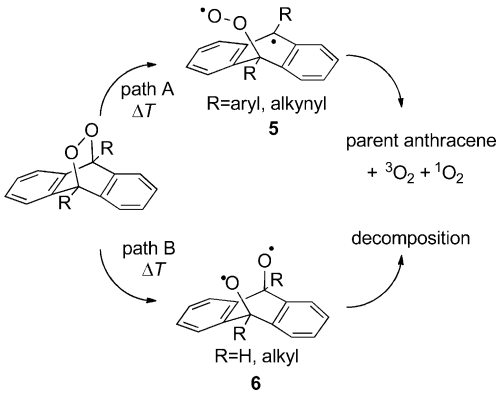


Figure 3. Comparison of the rates of EPO formation (□) and the $^1O_2$-releasing retro-reaction (■) for alkynylanthracene **1b**, DMN, and DPA at room temperature after 120 min.

The decay curves of alkynylanthracenes **1**, anthracene, and DMN are in the same range, whereas the reactivity of DPA is significantly higher. Inspection of the slopes within the series of substituted alkynylanthracenes discloses a strong dependence of the reactivity on the substituent. For example, derivative **1b**, which has electron-donating methoxy groups, reacts faster than derivative **1f**, which has an electron-withdrawing cyano group.

The requirements for a good chemical source of $^1O_2$ are the fast generation of the donor form and a high propensity to release $^1O_2$. These features are depicted by a comparison of **1b-O$_2$**, DMN, and DPA in Figure 3. We determined the conversion from the acene to the EPO after 120 min and the degree of reconversion by release of $^1O_2$ after 120 min. It becomes clear that DPA is rapidly converted into an EPO, but the release of $^1O_2$ at room temperature is not detectable. In contrast, the reconversion of DMN-O_2 is noticeable at room temperature, but formation of the EPO proceeded very slowly. Conversely, alkynylanthracene **1b** behaved exceptionally well; the transformation to the EPO was almost quantitative after 120 min and the retro-reaction of EPO **1b-O$_2$** was the fastest of the three donors. In summary, **1b-O$_2$** is a very good $^1O_2$ source that is also generated rapidly.

Although the reactivity of the forward reaction of alkynylanthracenes is tunable by the choice of the *para* substituent, no substituent effects apply for the reverse reaction. This observation can be explained by two different mechanistic pathways, namely a concerted one for the forward and a radical pathway for the reverse reaction.[24] The striking difference in reactivity of the reverse reaction between aryl and alkynyl substituents can be rationalized by consideration of a stepwise process with radical intermediates (Scheme 5).[12] Both aryl and alkynyl groups provide sufficient radical stabilization energy (RSE) to favor the formation of carbon radical **5**, which results from a C–O cleavage



Scheme 5. Proposed pathways for the thermolysis of EPOs.

(path A).[16,25] For R = H and alkyl groups, an O–O cleavage to form intermediate **6** is favored (path B), followed by decomposition.[17] To further support this hypothesis, we performed theoretical calculations at the HF/6-31G* level.[16] Local minima were found for intermediates **5** (R = Ph, alkynyl), whereas diradicals **6** gave no energetic minima and directly rearranged. Additionally, our isodesmic calculations showed that alkynyl groups have a smaller RSE than aryl groups,[16] in good agreement with the literature.[26] This explains the short lifetime of alkynyl-substituted diradical **5** (compared with R = Ph) and its faster release and higher yields of $^1O_2$.

In conclusion, we have shown that alkynylanthracenes **1** belong to a rare class of anthracenes that reversibly react to

form their corresponding **1-O_2** EPOs on a short timescale. The yield of $^1O_2$ is high and the release of oxygen is faster than for all other known types of acene EPOs. Given that even the rate to generate the EPO form is moderate, this class of compounds is well suited to act as a source of $^1O_2$ under mild conditions.

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Keywords: anthracenes · oxidation · peroxides · reversibility · singlet oxygen

[1] a) T. Linker, L. Fröhlich, *J. Am. Chem. Soc.* **1995**, *117*, 2694–2697; b) W. Fudickar, K. Vorndran, T. Linker, *Tetrahedron* **2006**, *62*, 10639–10646; c) M. Tofi, K. Koltsida, G. Vassilikogiannakis, *Org. Lett.* **2009**, *11*, 313–316; d) K. C. Nicolaou, S. Totokotsopoulos, D. Giguere, Y.-P. Sun, D Sarlah, *J. Am. Chem. Soc.* **2011**, *133*, 8150–8153; e) for a review, see: M. Prein, W. Adam, *Angew. Chem.* **1996**, *108*, 519–538; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 477–494.

[2] D. E. Dolmans, D. Fukumura, R. K. Jain, *Nat. Rev. Cancer* **2003**, *3*, 380–387.

[3] R. C. R. Wootton, R. Fortt, A. J. de Mello, *Org. Process Res. Dev.* **2002**, *6*, 187–189.

[4] a) H. Ito, T. Ikeda, K. O. Ichimura, *Macromolecules* **1993**, *26*, 4533–4538; b) W. Fudickar, T. Linker, *Langmuir* **2010**, *26*, 4421–4428.

[5] a) T. Matsuura, N. Yoshimura, A. Nishinaga, I. Saito, *Tetrahedron* **1972**, *28*, 4933–4938; b) V. S. Srinivasan, D. Podolski, N. J. Westrick, D. C. Neckers, *J. Am. Chem. Soc.* **1978**, *100*, 6513–6515; c) I. Saito, T. Matsuura, K. Inoue, *J. Am. Chem. Soc.* **1983**, *105*, 3200–3206; d) R. C. Kanner, C. S. Foote, *J. Am. Chem. Soc.* **1992**, *114*, 682–688; e) E. Baciocchi, T. D. Giacco, A. Lapi, *Org. Lett.* **2004**, *6*, 4791–4794.

[6] a) C. Pierlot, J.-M. Aubry, K. Briviba, H. Sies, P. di Mascio, *Methods Enzymol.* **2000**, *319*, 3–20; b) M. Nakano, Y. Kambayashi, H. Tatsuzawa, *Methods Enzymol.* **2000**, *319*, 216–222; c) M. J. Davies, *Biochem. Biophys. Res. Commun.* **2003**, *305*, 761–770; d) K. Otsu, K. Sato, Y. Ikeda, H. Imai, Y. Nakagawa, Y. Ohiba, J. Fujii, *Biochem. J.* **2005**, *389*, 197–206.

[7] a) G. Günther, E. Lemp, A. L. Zanocco, *J. Photochem. Photobiol. A* **2002**, *151*, 1–5; b) C. Pierlot, V. Nardello, R. Schmidt, J.-M. Aubry, *Arkivoc* **2007**, *VIII*, 245–256.

[8] a) C. S. Foote, S. Wexler, W. Ando, *J. Am. Chem. Soc.* **1968**, *90*, 975–978; b) V. Nardello, J. Barbillat, J. Marko, P. T. Witte, P. L. Alsters, J.-M. Aubry, *Chem. Eur. J.* **2003**, *9*, 435–441; c) J.-M. Aubry, *J. Am. Chem. Soc.* **1985**, *107*, 5844–5849.

[9] a) H. H. Wassermann, D. L. Larsen, *J. Chem. Soc. Chem. Commun.* **1972**, 253–254; b) C. Pierlot, S. Hajjama, C. Barthélémy, J.-M. Aubry, *J. Photochem. Photobiol. B* **1996**, *36*, 31–39; c) G. R. Martinez, J.-L. Ravanat, M. H. G. Medeiros, J. Cadet, P. di Mascio, *J. Am. Chem. Soc.* **2000**, *122*, 10212–10213; d) S. Ben-Shabat, Y. Itagaki, S. Jockusch, J. R. Sparrow, N. J. Turro, K. Nakanishi, *Angew. Chem.* **2002**, *114*, 842–845; *Angew. Chem. Int. Ed.* **2002**, *41*, 814–817.

[10] a) H. H. Wasserman, J. R. Scheffer, J. L. Cooper, *J. Am. Chem. Soc.* **1972**, *94*, 4991–4996; b) H. H. Wassermann, T. Y. Ching, B. H. Lipshutz, H. Matsuyama, F. E. Scully, Jr., P. Wang, *Bioorg. Med. Chem. Lett.* **1992**, *2*, 1137–1140; c) L. Slavetinska, J. Mosinger, M. Dracinsky, M. Posra, *J. Inclusion Phenom. Macrocyclic Chem.* **2008**, *61*, 241–250.

[11] J.-M. Aubry, C. Pierlot, J. Rigaudy, R. Schmidt, *Acc. Chem. Res.* **2003**, *36*, 668–675.

[12] W. Fudickar, T. Linker, *Chem. Commun.* **2008**, 1771–1773.

[13] For examples for other chemical sources of $^1O_2$, see: a) M. Matsumoto, M. Yamada, N. Watanabe, *Chem. Commun.* **2005**, 483–485; b) P. Ghorai, P. Dussault, *Org. Lett.* **2009**, *11*, 4572–4575.

[14] P. Nguyen, S. Todd, D. Van den Biggelaar, N. J. Taylor, T. B. Marder, F. Wittmann, R. Friend, *Synlett* **1994**, 299–301.

[15] S. Fraysse, C. Coudret, J.-P. Launay, *J. Am. Chem. Soc.* **2003**, *125*, 5880–5888.

[16] See the Supporting Information for details.

[17] a) P. F. Southern, W. A. Waters, *J. Chem. Soc.* **1960**, 4340–4346; b) J. Rigaudy, J. Baranne-Lafont, A. Defoin, N. K. Cuong, *Tetrahedron* **1978**, *34*, 73–82; c) J. Rigaudy, A. Defoin, J. Baranne-Lafont, *Angew. Chem.* **1979**, *91*, 443–444; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 413–415.

[18] N. J. Turro, M.-F. Chow, J. Rigaudy, *J. Am. Chem. Soc.* **1981**, *103*, 7218–7224.

[19] D. F. Evans, J. N. Tucker, *J. Chem. Soc. Faraday Trans. 2* **1976**, *72*, 1661–1664.

[20] M. Schäfer-Ridder, U. Brocker, E. Vogel, *Angew. Chem.* **1976**, *88*, 262–267; *Angew. Chem. Int. Ed. Engl.* **1976**, *15*, 228–229.

[21] Some EPOs of imidazoles reconvert to the parent heterocycle at temperatures $> -30\,^{\circ}C$ and are, therefore, not isolable, see: H.-S. Ryang, C. S. Foote, *J. Am. Chem. Soc.* **1979**, *101*, 6683–6687.

[22] Y. Nagaoka, K. Otsu, F. Okada, K. Sato, Y. Ohba, N. Kotani, J. Fujii, *Biochem. Biophys. Res. Commun.* **2005**, *331*, 215–223.

[23] B. Stevens, S. R. Perez, J. A. Ors, *J. Am. Chem. Soc.* **1974**, *96*, 6846–6850.

[24] a) G. A. Leach, K. N. Houk, *Chem. Commun.* **2002**, 1243–1255; b) A. R. Reddy, M. Bendikov, *Chem. Commun.* **2006**, 1179–1180.

[25] The RSEs of the alkyl, aryl, and alkynyl groups are 13, 72, and 58 kJ mol^{-1}, respectively; see also ref. [26].

[26] M. L. Coote, C. Y. Lin, H. Zipse in *Wiley Series on Reactive Intermediates in Chemistry, Vol. 3, Carbon-Centered Free Radicals and Radical Cations* (Eds.: E. Rokita, M. D. E. Forbes), Wiley, New York, **2010**, Chapter 5, pp. 83–102.

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