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Competition Between Cα-S and Cα-Cβ Bond Cleavage in β-Hydroxy sulfides Cation Radicals Generated by Photoinduced Electron Transfer†

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ABSTRACT

A kinetic and product study of the 3-cyano-N-methyl-quinolinium photoinduced mono-electronic oxidation of a series of β-hydroxy sulfides has been carried out to investigate the competition between Cα-S and Cα-Cβ bond cleavage within the corresponding cation radicals. Laser flash photolysis experiments unequivocally established the formation of sulfoxide cation radicals showing their absorption band (λmax ≈ 520 nm) and that of 3-CN-NMQ (λmax ≈ 390 nm). Steady-state photolysis experiments suggest that, in contrast to what previously observed for alkyl phenyl sulfide cation radicals that exclusively undergo Cα-S bond cleavage, the presence of a β-hydroxy group makes, in some cases, the Cα-Cβ scission competitive. The factors governing this competition seem to depend on the relative stability of the fragments formed from the two bond scissions. Substitution of the β-OH group with -OME did not dramatically change the reactivity pattern of the cation radicals thus suggesting that the observed favorable effect of the hydroxy group on the Cα-Cβ bond cleavage mainly resides on its capability to stabilize the carboxylation formed upon this scission.

INTRODUCTION

It is a great honor for us for having been invited to contribute to the Special Issue of Photochemistry & Photobiology dedicated to celebrating the career of Dr. Edward Clennan. Because of Ed’s fundamental contribution to the photochemistry of sulfur-containing compounds, it is a pleasure to present here our work concerning the one-electron photooxidation of β-hydroxy sulfides promoted by 3-cyano-N-methyl-quinolinium.

It is well known that electron transfer (ET) processes play a fundamental role in many biological and organic processes. For this reason, an increasing number of studies have been focused on the reactivity and the properties of the radical ions, the primary species obtained from these processes (1,2). Among the classes of organic compounds whose reactivity in ET process have been the subject of intense investigation, sulfides have attracted a special interest (3–8) since their mono-electronic oxidation is involved in many biological processes (9), in organic synthesis (10) and in the initiation of radical polymerization (11). To better elucidate the reaction mechanisms involved in sulfides oxidation initiated by an ET process, the use of photosensitizers as initiators has been widely employed particularly in type I (12) sulfide photooxygenation (6,13,14). Despite the large number of studies on the monoelectronic oxidation of organic sulfides, the same process on their oxidized form, organic sulfoxides, is much less investigated albeit, in the past decades, the comprehension of their reactivity and properties has attracted the interest of several research groups since sulfoxides are involved in many synthetic and biological processes (15–19). The main reason for the scarce information on the reactivity and properties of sulfide cation radicals is due to the fact that sulfoxides generally exhibit redox potentials 0.5 V higher than those of the corresponding sulfides (20,21) making them less prone to undergo mono-electronic oxidation. As an example, the redox potentials of methyl phenyl sulfoxide and thioanisole are 2.01 (21) and 1.47 V (22) (vs SCE), respectively.

Previous studies on the reactivity of alkyl aryl sulfoxide cation radicals (ArSOR••) have shown that the fate of these oxidized species largely depends on the nature of the alkyl substituent R. When R is a methyl or a primary alkyl group (except the benzyl group), once formed by photosensitized oxidation, the sulfoxide cation radical undergoes unproductive back electron transfer (BET) (21). When R is a benzylic, secondary or tertiary alkyl group, the cation radical undergoes Cα-S bond cleavage affording the R+ carboxylation and the phenyl sulfinyl radical ArSO• (Scheme 1) (23–25).
The $C_6S$ bond cleavage is a peculiar process characterizing both sulfide and sulfoxide cation radicals (23–34) since the fragmentation of cation radicals of other classes of organic compounds often involves the bonds in $\beta$ position with respect to the charged center. In a previous study, on the reactivity of aryl sulfoxide cation radicals bearing a hydroxy group in $\beta$ position, we showed that the OH group determines the $C_6S$ bond cleavage (35). The favorable effect of the hydroxy group on the $C_6S$ bond cleavage was proposed to be due to a transition state stabilization by a hydrogen bonding between the OH and the solvent (MeCN). In view of the above-mentioned higher redox potential of sulfoxides with respect to sulfides and of the higher stability of the phenyl sulfanyl radical PhSO$^+$ as compared to the phenylthiyl radical PhS$^+$ (36), the $C_6S$ bond cleavage is very much faster for sulfoxide cation radicals rather than for sulfide radicals (24,35), thus competition between $C_6S$ and $C_6C$ bond cleavage for $\beta$-hydroxy sulfoxides cation radicals can be foreseen. On these bases, we now report a kinetic and product study of the fragmentation process of a series of $\beta$-hydroxysulfoxides (Chart I) cation radicals. To better understand the role played by the $\beta$-hydroxy group, the investigation was also extended to two $\beta$-methoxy sulfoxides (5 and 6).

The cation radicals were generated by photosensitized monoelectronic oxidation of the parent $\beta$-hydroxysulfoxides as already reported in previous studies on the reactivity of aryl sulfoxide cation radicals (21,23–25). The photosensitizer chosen for this purpose was the 3-cyano-N-methylquinolinium perchlorate (3-CN-NMQ$^+$ ClO$_4^-$, Scheme 2) for the following reasons: (1) it is a powerful oxidant in its excited singlet state having a reduction potential of 2.72 V vs SCE in MeCN (37); (2) the $^{1}$[3-CN-NMQ$^+$]$^*$ lifetime is sufficiently long ($\tau = 45$ ns) (37) to efficiently interact with the substrates investigated; (3) the UV absorption maximum of 3-CN-NMQ$^+$ at ca 330 nm allows a selective photosensitizer excitation thus avoiding a direct photolysis of the sulfoxides 1–6 which absorb below 320 nm. Finally, since the photosensitizer is positively charged, upon the ET process a cation radical/radical couple is formed with a consequent easier separation of the two species (lack of electrostatic barrier) thus depressing the unproductive BET process.

**Scheme 1.** $C_6S$ bond cleavage in alkyl aryl sulfoxide cation radicals.

**Chart 1.** $\beta$-hydroxy and $\beta$-methoxy sulfoxides investigated in this work.
was obtained as a white solid. $^1$H and $^{13}$C NMR analysis are in agreement with those reported in ref. (45).

$^1$H NMR (CDCl₃) δ (ppm): 7.45-7.05 (m, 10H), 4.70 (dq, 1H, J = 6.6 Hz, J = 2.94 Hz), 3.63 (d, 1H, J = 2.94 Hz), 1.03 (d, 3H, J = 6.45 Hz).

$^{13}$C NMR (CDCl₃) δ (ppm): 131.9, 131.8, 131.6, 131.5, 129.5, 129.1, 128.7, 128.4, 126, 125.4, 78.7, 75.0, 60.2, 21.6.

Synthesis of 1-[1-methoxy-1-phenylpropyl]sulfinyl]benzene (5). To a stirred suspension of NaH (281 mg, 12 mmol) in anhydrous THF (10 mL), 1-phenyl-2,4-diphenylsulfonylpropan-1-ol (1.2 g, 4.9 mmol) was slowly added under an Ar atmosphere. After 30 min stirring at room temperature, CH₃I (1.7 g, 12 mmol) was slowly added and the mixture was then allowed to react overnight. After water addition (50 mL), the mixture was concentrated at reduced pressure, solubilized in diethyl ether (100 mL), washed twice with water (50 mL), dried over anhydrous Na₂SO₄, and the mixture was stirred for 3 h. After water addition (20 mL), the mixture was washed twice with water (50 mL), dried over anhydrous Na₂SO₄, and the mixture was then concentrated at reduced pressure, then washed with anhydrous MeCN and washed at 5°C. The following results are thus referred to the stereoisomers mixture for compounds 1–6.

RESULTS AND DISCUSSION

The sulfoxides investigated in this work contain two (1 and 3) or three (2, 4, 5 and 6) chiral centers. The following results are thus referred to the stereoisomers mixture for compounds 1–6.

Electrochemical properties

Sulfoxides 1–6 were electrochemically characterized by cyclic voltammetry experiments. The experiments were carried out on a solution of 1–6 (2 mM) in dry MeCN under inert atmosphere at 25 °C, using Bu₄NBF₄ (0.1 M) as support electrolyte, an Ag/AgCl (KCl 3 M) reference electrode with a 0.5 V s⁻¹ scan rate. For all the sulfoxides investigated an irreversible oxidation process was observed even at higher scan rates (up to 5 V s⁻¹) as described in Fig. 1 for 3 (see Figures S1–S5 for the voltammograms of 2–6). Because of the irreversibility observed, only the anodic peak potential values ($E^p_a$) were determined, and their values (vs SCE) are reported in Table 1.

The measured $E^p_a$ values span from 1.77 to 2.04 V for 4 and 1, respectively, with the latter very similar to that measured for methyl phenyl sulfoxide under the same experimental conditions ($E^p_a = 2.01$ V vs SCE) (21). The differences of $E^p_a$ values for the sulfoxides 1–6 are very likely due to the ability of the α-alkyl...
group to stabilize the cation radical in which both the charge and the spin density are mainly located on the sulfinyl group (21). Accordingly in 1, the primary alkyl group should have a stabilizing effect closer to that observed for the methyl group in methyl phenyl sulfoxide whereas for 2–6 the higher degree of substitution should better stabilize the cation radical thus decreasing the oxidation potential. Comparing the $E_p^a$ values of 2–3 with those of the corresponding methyl ethers (5 and 6, respectively), it appears that in both cases the substitution of the hydroxy with a methoxy group is reflected in a slight decrease of the oxidation potential ($\Delta E_p^a = 0.05 \text{ V}$). This is probably due to the presence of an intramolecular hydrogen bonding between the hydroxy group and the sulfinyl oxygen atom which determines a decrease of the electron density on the sulfinyl group thus increasing the oxidation potential. In all cases, the $E_p^a$ values reported in Table 1 are largely below the $[3\text{-CN-NMQ}^+]^*$ reduction potential (2.72 V vs. SCE in MeCN) (37) thus allowing an exergonic ET process with all the examined sulfoxides. Accordingly, by applying the Weller equation (50), it results that for all the sulfoxides $\Delta G_{\text{ET}} < -16 \text{ kcal mol}^{-1}$.

**Fluorescence quenching experiments**

Having established the thermodynamic feasibility of the ET process from sulfoxides 1–6 to $[3\text{-CN-NMQ}^+]^*$, fluorescence quenching experiments were performed in order to determine the rate constants of the interaction of $[3\text{-CN-NMQ}^+]^*$ with the substrates investigated. The measurements were carried out irradiating a deaerated MeCN solution of 3-CN-NMQ$^+$ (1.7 $\times$ 10$^{-5}$ M) at its absorption maximum wavelength ($\lambda_{\text{max}} = 330 \text{ nm}$) and following the decrease of the emission at its maximum intensity ($\lambda_{\text{max}} = 425 \text{ nm}$) on increasing the sulfoxide concentration (from 2 $\times$ 10$^{-4}$ to 0.01 M). According to the Stern-Volmer equation, by plotting the ($I_0/I$)-1 vs the sulfoxide concentration, very good linear plots were obtained (Figures S6–S10) from whose slopes the fluorescence quenching kinetic constants ($k_q$) were obtained (Table 1). For all the sulfoxides examined the rate constant for the $[3\text{-CN-NMQ}^+]^*$ quenching is close to the diffusion limit in MeCN (1.9 $\times$ 10$^{10}$ M$^{-1}$ s$^{-1}$) (51) in agreement with a photoinduced ET process.

**Steady-state photolysis: product study**

Steady-state photolysis experiments were carried out irradiating an Ar-saturated MeCN solution (5 mL) of the sulfoxide (1 $\times$ 10$^{-2}$ M) and 3-CN-NMQ$^+$ ClO$_4^-$ (2 $\times$ 10$^{-3}$ M) at 25 °C in a photoreactor equipped with four fluorescence lamps with a maximum emission at 360 nm. At this wavelength, only the photosensitizer is excited as confirmed by the total absence of oxidation products observed in blank experiments where substrates solutions were irradiated in the absence of the photosensitizer. All the reaction products were identified and characterized by $^1$H NMR and GC-MS analysis (comparison with authentic specimens and literature data). Product quantitative analysis was performed by $^1$H NMR and GC (products derived from alkyl

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**Table 1.** Anodic peak potentials for 1-6 and rate constants ($k_q$) for the fluorescence quenching of $[3\text{-CN-NMQ}^+]^*$ by 1-5.

| Sulfoxide | $E_p^a$ (V) vs SCE | $k_q$ ($\times$ 10$^{10}$ M$^{-1}$ s$^{-1}$) |
|-----------|-------------------|-----------------------------------|
| 1         | 2.04              | 1.35                              |
| 2         | 1.89              | 1.69                              |
| 3         | 1.85              | 1.32                              |
| 4         | 1.77              | 0.52                              |
| 5         | 1.84              | 0.73                              |
| 6         | 1.80              |                                    |

$^1$In MeCN at 25 °C using an Ag/AgCl (KCl 3 m) as the reference electrode. $^2$In MeCN at 25 °C.
fragments) and HPLC (sulfur-containing products). In all cases, the overall material recovery was satisfactory (> 90%).

After irradiation of the β-hydroxy sulfoxide 1, product analysis did not show the presence of any reaction product even after prolonging the irradiation time to two hours whereas irradiation of 2 led, after only 10 min, to significant amounts of fragmentation reaction products, that is, benzaldehyde, benzyl methyl ketone, diphenyl disulfide and phenyl phenylthiosulfonate (entries 1 and 2 in Table 2). On increasing the irradiation time to 30 min the same reaction products were observed with higher yields but they were accompanied by other unknown products probably derived from overoxidation. In Table 2, products and yields for the photosensitized oxidation of the corresponding methyl ether 5 under the same reaction condition are also reported (entries 3 and 4). The products observed are the same as for 2 with the additional formation of 1-phenyl-2-methoxy-1-propanol and, after the same irradiation time (10 min), the overall no sulfur-containing product yields for 5 (3.4%) is slightly higher than that for 2 (2.6%).

When the β-hydroxy sulfoxide 3 was irradiated under the same reaction condition of 2, beside the same sulfur-containing fragmentation products observed for 2, 2-phenyl-2-methylpropanal was the exclusive product deriving from the alkyl moiety (entries 5 and 6 in Table 2). As already observed for 2, also for 3 a prolongation of the irradiation time to 30 min resulted in the formation of the same reaction products in higher yields but accompanied by unidentified products. A comparison with the results obtained with 2 shows a significantly increased product yield for the photosensitized oxidation of 3 with the overall yield, for the fragmentation products deriving from the alkyl moiety, passing from 2.6% to 11% after 10 min irradiation for 2 and 3, respectively. The photooxidation of the corresponding methyl ether 6 afforded the same fragmentation products observed for 3 but with slightly higher yields (entries 7 and 8 in Table 2).

A 10 min irradiation of the β-hydroxy sulfoxide 4 under the same reaction condition as for 2 and 3, leads to the formation of the fragmentation products (entry 9 in Table 2): benzaldehyde and diphenylacetaldehyde from the alkyl moiety, diphenyl disulfide and phenyl phenylthiosulfonate from the sulfur-containing one. Comparison between entry 9 with entries 1 and 5 in Table 2, shows that the photooxidation of 4 is more efficient than those of 2 and 3 with an overall yield for products deriving from the alkyl moiety of 20%.

Laser flash photolysis study

To have a deeper insight in both the nature and the reactivity of the reaction intermediates involved in these processes, a laser flash photolysis (LFP) investigation was carried out. LFP experiments were carried out in N2-saturated MeCN at 22 °C in the presence of 1 M toluene as cosensitizer to minimize the BET process and thus increasing the cation radical yield (52). For all the substrates investigated, the time-resolved absorption spectra show the formation of two transient species absorbing at ca 390 and 520 nm, respectively (Fig. 2, for 3 and Figures S11–S15 for 1, 2, 4, 5, and 6). On the basis of the absorption spectra of aromatic sulfoxide cation radicals reported in the literature (21,24), the absorption band at 520 nm can be assigned to the 3-CN-NMQ+ radical (24).

The observed intermediates confirm the occurrence of an ET process, from the sulfoxides to the singlet excited state of 3-CN-NMQ+, as the main reaction process (Scheme 2). Interestingly,

| Table 2. Products and yields for the 3-CN-NMQ+ photosensitized oxidation of sulfoxides 1-6 in MeCN at 25 °C. |
|---|---|---|---|---|---|
| Entry | Compound | t (min) | Products and yields (%)† |
| 1 | 2 | 10 | 0.4 | 1.3 | 0.5 | 2.1 |
| 2 | 3 | 30 | 1.2 | 4.3 | 2.2 | 10 |
| 3 | 5 | 10 | 0.5 | 1.6 | 0.8 | 0.6 | 2.0 |
| 4 | 5 | 30 | 1.6 | 4.8 | 1.9 | 2.0 | 9.2 |
| 5 | 3 | 10 | 0.6 | 5.4 | 11 |
| 6 | 3 | 30 | 2.5 | 6.6 | 18 |
| 7 | 6 | 10 | 0.8 | 5.9 | 13 |
| 8 | 6 | 30 | 3.1 | 7.8 | 21 |
| 9 | 4 | 10 | 1.4 | 4.7 | 13 | 6.8 |

†Yields, average of at least two independent determinations, are referred to the initial amount of substrate.
the absorbance decay at 520 nm does not follow the same kinetic order for all of the substrates. A clean 1st order kinetic profile is only observed for 3**, 4** and 6** (Fig. 2 for 3 and Figures S13 and S15 for 4 and 6) whereas the other cation radicals show a 2nd order (1**) or a mixed 1st–2nd order (2** and 5**) kinetic profile (Figures S11, S12 and S14). This observation suggests that only 3**, 4** and 6** mainly undergo unimolecular fragmentation process whereas for the other cation radicals their decay is partially (2** and 5**) or totally (1**) associated with a BET process. Such a different behavior is in full agreement with the steady-state photolysis experiments results (Table 2) where product yields for 3, 4 and 6 (entries 5, 7 and 9), for which the unproductive BET poorly competes with the fragmentation process, are significantly higher than those for 2 and 5 (entries 1 and 3). Accordingly, 1, whose cation radical exclusively undergoes BET, was unreactive even at prolonged irradiation times. The values of the 1st order rate constants, \( k_{\text{frag}} \), obtained for 3**, 4** and 6** are reported in Table 3.

Comparison between the \( k_{\text{frag}} \) values for 3** and 6** shows that the presence of the \( \beta \)-methoxy group slightly speeds up the cation radical fragmentation process with respect to the \( \beta \)-hydroxy group. The reason for the lower fragmentation rate observed for 3** could be tentatively attributed to a slight stabilizing effect related to the presence of an intramolecular hydrogen bond between the \( \beta \)-hydroxy group and the oxygen-centered radical as recently reported for the stabilizing effect of alkoxyl radicals by hydrogen bonding (53). Interestingly, the higher fragmentation rate constant observed for 6** seems to be reflected in the slightly higher product yields observed in the photooxidation of 6 with respect to those for 3 (Compare entries 5 and 7 in Table 2). Indeed, a higher fragmentation rate makes this process more competitive toward the unproductive BET. In the same way, the significantly faster fragmentation process of 4**, with respect to those of 3** and 6**, accounts for the higher product yields observed in the photooxidation of 4 (compare entries 5 and 9 in Table 2).

**DISCUSSION**

The results obtained in the 3-CN-NMQ\(^+\) photosensitized oxidation of sulfoxides 2–6 show the formation of significant amount of fragmentation products. No products were observed in the oxidation of 1, a result that can be attributed to the low fragmentation rate for the cation radical 1** that favors the competitive and unproductive BET process as shown by the LFP experiments. For 1**, the \( C_\text{S} \)-S bond cleavage rate is expected to be slower than those for the cation radicals 2**–6** because of the primary alkyl group bonded to the sulfur atom. Moreover, the
presence of the \(\beta\)-OH group seems not to be able to induce an efficient \(C_{\alpha}C_{\beta}\) bond fragmentation as observed for the \(\beta\)-hydroxy sulfides (35).

In a previous study, it was observed that the presence of bases, that is, substituted pyridines, in the reaction medium is reflected in a dramatic acceleration of the \(C_{\alpha}C_{\beta}\) bond cleavage in \(\beta\)-hydroxysulfide cation radicals (35). Such acceleration was rationalized invoking a transition state where the \(C_{\alpha}C_{\beta}\) bond cleavage and the intramolecular ET from this bond to the sulfur atom are coupled with the O-H bond cleavage induced by the base. On these bases, we carried out some 3-CN-NMQ\(^+\) photosensitized oxidation reactions on 1 in the presence of pyridine (from 0.001 to 0.1 M) or 4-CN-pyridine (from 0.02 to 0.1 M) in order to induce the \(C_{\alpha}C_{\beta}\) bond cleavage but, also under these reaction conditions, no reaction products were observed. The lack of oxidation products observed also in the presence of pyridines may be likely due to the possibility that these species could favorably compete with 1 in the ET process to the excited sensitizer. In contrast, when more oxidizable sulfides are used as substrates, this possibility can be excluded.

In the oxidation of the \(\beta\)-hydroxysulfoxide 2, two fragmentation products deriving from the alkyl moiety (benzaldehyde and phenylacetone) are observed accompanied by two sulfur-containing ones, that is, diphenyl disulfide and phenyl phenylthiosulfonate. The formation of these products suggests that both \(C_{\alpha}C_{\beta}\) and \(C_{\alpha}S\) bond cleavage take place on 2\(^+\) as described in Scheme 3. According to the proposed mechanism, phenylacetone derives from the \(C_{\alpha}S\) bond scission (path a) whereas benzaldehyde derives from the \(C_{\alpha}C_{\beta}\) scission (path b). The mechanism for the formation of phenylacetone from the carbocation \(\text{C}_6\text{H}_5\text{CH(OH)}\text{CH}^+\text{CH}_3\) involves the conversion of the latter into a protonated epoxide (path c) followed by a 1,2- hydride shift (path d) as already reported (54). Since benzaldehyde and phenylacetone come from competitive \(C_{\alpha}C_{\beta}\) and \(C_{\alpha}S\) bond cleavage, respectively, from their molar ratio (see entry 1 in Table 2) it is possible to estimate the relative rates for these two processes with the \(C_{\alpha}S\) bond cleavage being ca 4 fold faster than \(C_{\alpha}C_{\beta}\) one.

The sulfur-containing products observed in the photooxidation of 2\(^+\) are those expected to derive from the phenyl sulfinyl radical formed upon \(C_{\alpha}S\) bond scission. Accordingly, the same products were already observed in previous studies concerning the photosensitized oxidation of alkyl aryl sulfoxides (24), and their formation was proposed to involve the first reduction of the phenyl sulfinyl radical to phenyl sulfenate by the reduced form of 3-cyano-N-methyl-quinolinium, 3-CN-NMQ\(^+\) (Scheme 4, path a). This process is thermodynamically favored since the reduction potential of PhSO\(^-\) (1.08 V vs SCE in MeCN) (24) is much higher than that of 3-CN-NMQ\(^+\) (−0.60 V vs SCE in MeCN) (55) and accounts for the high photosensitizer recovery observed in the reaction mixtures after irradiation (> 77%). Once formed, the sulfenate anion or its protonated form, sulfenic acid, are converted to the observed products PhSSPh and PhSO\(_2\)SPh as described in Scheme 4 (36).

As described in Scheme 3 (path b), the \(C_{\alpha}C_{\beta}\) bond cleavage on 2\(^+\) leads to the formation, besides benzaldehyde, of an \(\alpha\)-sulfinylmethyl radical. Since there was no evidence for the formation of its dimerization product, a possible fate for this species.

![Scheme 3](image-url) Scheme 3. Plausible mechanism for product formation from 2\(^+\). Framed structures represent the observed reaction products deriving from \(C_{\alpha}C_{\beta}\) (red) and \(C_{\alpha}S\) bond cleavage (blue) or both (black).
could involve its oxidation to the corresponding carbocation followed by reaction with trace of water to form sulfenic acid (and then PhSSPh and PhSO₂SPh) and acetaldehyde (Scheme 3, path e). The photoinduced oxidation of the β-methoxy sulfoxide 5 provides the same reaction products observed for the corresponding β-hydroxy sulfoxide 2 accompanied by a significant amount of 2-methoxy-1-phenyl-1-propanol. According to the mechanism proposed for 2 (Scheme 3), product formation from 5 can be rationalized as described in Scheme 5 where the carbocation deriving from the Cα-S bond cleavage (path a) can be converted into an oxiranium intermediate (path c) that can undergo both nucleophilic water addition (path d) to give 2-methoxy-1-phenyl-1-propanol or 1,2-hydride shift (path e) to provide a carbocation precursor of benzyl methyl ketone. The alkyl fragment deriving from the Cα-Cβ bond cleavage (path b), after water addition, provides the hemiacetal precursor of benzaldehyde. On the basis of

**Scheme 4.** Proposed mechanism for the conversion of the phenyl sulfinyl radical to the sulfur-containing products observed in the photooxidation of 2-6 sensitized by 3-CN-NMQ⁺.

**Scheme 5.** Proposed mechanism for product formation from 5++. Framed structures represent the observed reaction products deriving from Cα-Cβ (red) and Cα-S bond cleavage (blue).
the relative amount of 2-methoxy-1-phenyl-1-propanol, benzyl methyl ketone and benzaldehyde (Table 2), a significant predominance of Cα-S over Cα-Cβ bond cleavage seems to take place within 5**.

The photooxidation of 3 and 6, afforded 2-methyl-2-phenylpropanal as the exclusive product deriving from the alkyl moiety whereas the sulfur-containing products were the same as observed for 2: diphenyl disulfide and phenyl phenythiosulfonate (Table 2, entries 5–8). This result suggests the occurrence of Cα-S bond cleavage as the exclusive fragmentation process for 3** and 6** (Scheme 6). The formation of 2-methyl-2-phenylpropanal from 3** and 6** can be rationalized taking into account a 1,2-phenyl shift within the carbocation thus formed (Scheme 6, path a for 3**) as already reported (54).

The formation of diphenylacetaldehyde, and benzaldehyde from the alkyl moiety, and diphenyl disulfide and phenyl phenythiosulfonate as sulfur-containing products (Table 2, entry 9) in the photooxidation of 4 suggests that 4** can undergo both Cα-S and Cα-Cβ bond cleavage as described in Scheme 7 where diphenylacetaldehyde derives from the Cα-S scission (path a) followed by a 1,2-phenyl shift within the carbocation thus formed (path c) as previously proposed for 3** (54). In contrast, benzaldehyde is formed upon Cα-Cβ bond cleavage (path b) in a similar way as described for the same process with 2. Moreover, it should be considered that for 4** the Cα-Cβ bond cleavage leads not only to benzaldehyde but also to the formation of an α-sulfynyl radical that, upon further oxidation (path d), should convert to a sulfinic acid and a second benzaldehyde molecule following the pathway proposed above for 2**.

Under the assumption that two molecules of benzaldehyde are formed upon Cα-Cβ fragmentation, the corrected benzaldehyde and diphenylacetaldehyde yields ratio (Table 2, entry 9) indicates an almost equal percentage of Cα-Cβ and Cα-S bond cleavage thus suggesting that the presence of the α-phenyl group can stabilize the same extent both the secondary benzyl carbocation, from Cα-S scission, and the secondary benzylic α-sulfynyl radical deriving from the Cα-Cβ scission.

The collected results show that the presence of a β-hydroxy or -methoxy substituent in the sulfoxide cation radicals investigated renders the Cα-Cβ bond cleavage competitive with the Cα-S scission. The extent of this competition appears to be highly dependent on the relative stabilities of the fragments formed from these two processes. Since all the β-hydroxsulfoxide cation radicals afford two common fragments from the Cα-S and Cα-Cβ bond cleavage, that is, PhSO* and [PhCHOH]* respectively, the competition between these two processes is only governed by the relative stability of the other two fragments formed: PhCH(OH)C*‘RR’ from Cα-S fragmentation and PhSi(O)C*‘RR’ from Cα-Cβ bond cleavage. Thus, the exclusive Cα-S bond cleavage observed for 3** should be likely due to the stability of the tertiary carbocation formed that would result higher than that of the alkyl radical deriving from the Cα-Cβ scission. Moreover, the observation that the Cα-Cβ bond cleavage competes more favorably in 4** (Cα-S/Cα-Cβ ≈ 1) rather than in 2** (Cα-S/Cα-Cβ ≈ 4) suggests that the α-phenyl substituent would stabilize the radical fragment formed upon Cα-Cβ cleavage (PhS(O)C*‘HPh), with respect to the carbocation deriving from the Cα-S scission (PhCH(OH)CH*‘Ph), more efficiently than the α-methyl group. Accordingly, the lower stabilities of both the primary carbocation and radical that would have been formed from the Cα-S and Cα-Cβ bond cleavage in 1** determine a fragmentation rate too low to compete with the unproductive BET.

Concerning the role of the hydroxyl substituent on the cation radical fragmentation, both product analysis and LPF experiments on 2–5 and 3–6 show a negligible effect of the substitution of the -OH with the -OMe group. These observations suggest that the previously proposed favorable effect on the Cα-
Cβ bond cleavage, within β-hydroxysulfide cation radicals, exerted by a hydrogen bonding between the -OH and the solvent in the transition state (35) is no longer valid for β-hydroxysulfoxides. Thus, the favorable effect of the β-oxygenated substituents on the Cα-Cβ bond scission seems to be exclusively due to the stabilization of the formed carbocation, exerted by the vicinal oxygen atom.

To better investigate the role of a β-oxygenated group (-OH or -OMe) on the Cα-S bond cleavage within a sulfoxide cation radical, it could be worthy of interest to compare the $k_{tag}$ values for 3** and 6** with that of the t-butyl phenyl sulfoxide cation radical previously measured under the same experimental condition (24). As for 3** and 6**, the cation radical of t-butyl phenyl sulfoxide has a tertiary alkyl group bonded to the sulfur atom and was shown to exclusively undergo Cα-S bond cleavage with a rate constant of $1.6 \times 10^8$ s$^{-1}$, one order of magnitude higher than those measured for 3** and 6** (Table 3). Interestingly, the presence of the β-oxygenated substituent seems to stabilize the cation radical thus discarding a significant contribution of an intramolecular nucleophilic assistance, exerted by the β-OH or -OMe substituent, on the Cα-S bond cleavage. Such a stabilization could be associated with the formation of a two-center-three electrons intramolecular bond between the β-oxygen atom and the cation radical localized on the sulfanyl group, as previously proposed for the intermolecular stabilization of DMSO cation radical by water molecules (56).

CONCLUSION

All the β-hydroxysulfoxides investigated in this work have been shown to rapidly react with the singlet excited state of 3-CN-NMQ+ via an ET process affording the corresponding cation radicals as unequivocally revealed by LFP experiments. Once formed, the cation radicals can undergo either BET or fragmentation processes whose competition depends on the relative stability of the fragments formed in the latter process. Beside the expected Cα-S bond cleavage, product analysis in steady-state photolysis experiments showed, in some cases, the occurrence of the unprecedented Cα-Cβ bond scission as well. In this case too, the competition between these two fragmentation processes in β-hydroxysulfoxides cation radicals seems to depend mainly on the relative stability of the fragments formed. Finally, the similar behavior observed for the β-methoxysulfoxides 5 and 6 and the corresponding β-hydroxysulfoxides (2 and 3) in both LFP and steady-state experiments clearly indicates that the role of the β-hydroxy substituent in promoting the Cα-Cβ bond cleavage is limited to the stabilization of the α-carbocation formed. This evidence discards the hypothesis of a solvent assistance, via hydrogen bonding, previously proposed for the same process in β-hydroxysulfides cation radicals.

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REFERENCES

1. Eberson, L. (1987) Electron Transfer Reactions in Organic Chemistry. Springer, Berlin.
2. Balzani, E. V. (2001) Electron Transfer in Chemistry. Wiley-VCH, Weinheim.
3. Glass, R. S. (2018) Sulphur radicals and their application. Top. Curr. Chem. (Z) 376, 22.
4. Lanzalunga, O. and A. Lapi (2012) Recent photo- and radiation chemical studies of sulfur radical cations. J. sulfur Chem. 33, 101–129.
5. Glass, R. S. (1999) Organosulfur chemistry II. Top. Curr. Chem. 205, 1.
6. Bacciocchi, E., T. Del Giacco, F. Elisei, M. F. Gerini, M. Guerra, A. Lapi and P. Liberati (2003) Electron transfer and singlet oxygen mechanisms in the photoxoygenation of dibutyl sulphide and thioanisol in MeCN sensitized by N-methylquinolinium tetrafluoroborate and 9,10-dicyanoanthracene. The probable involvement of a thiadioxirane intermediate in electron transfer photoxoygenations. J. Am. Chem. Soc. 125, 16444–16454.
7. Filipiak, P., K. Bobrowski, G. L. Hug, D. Pogocki, C. Schönich and B. Marcinia (2016) Formation of a three-electron sulfur-sulfur bond as a probe for interaction between side chains of methionine residues. J. Phys. Chem. B 120, 9732–9744.
8. Ignasiak, M. T., T. Pedzinski, F. Rusconi, P. Filippiak, K. Bobrowski, C. Houé-Levin and B. Marcinia (2014) Photosensitized oxidation of methionine-containing dipeptides, from the transients to the final products. J. Phys. Chem. B 118, 8549–8558.
9. C. Chatgilialoglu and K. D. Asmus (eds.) (1990) Sulfur Centered Reactive Intermediates in Chemistry and Biology. Plenum Press, New York.
10. Albini, A., M. Fagnoni and M. Mella (2000) Environment-friendly organic synthesis. The photochemical approach. Pure Appl. Chem. 72, 1321–1326.
11. Wrzeszczyński, A., P. Filippiak, G. L. Hug, B. Macinia and J. Paczkowski (2000) Photoinduced electron transfer polymerization. 4. Carboxybenzophenone-sulfur-containing carboxylic acids photoedox pairs as a photoinitiating system for free-radical polymerization. Macromolecules 33, 1577–1582.
12. Baptista, M. S., J. Cadet, P. Di Mascio, A. A. Ghogare, A. Greer, M. R. Hamblin, C. Lorente, S. C. Nunez, M. Simões Ribeiro, A. H. Thomas, M. Vignon and T. Mateus Yoshimura (2017) Type I and Type II photosensitized oxidation reactions: guidelines and mechanistic pathways. Photochem. Photobiol. 93, 912–919.
13. Bonnesi, S. M., I. Manet, M. Freecero, M. Fagnoni and A. Albini (2006) Photosensitized oxidation of sulfides: discriminating between the singlet-oxygen mechanism and electron transfer involving superoxide anion or molecular oxygen. Chem. Eur. J. 12, 4844–4857.
14. Clennan, E. L. and C. Liao (2008) Role of sulfide radical cations in electron transfer promoted molecular oxygenation at sulfur. J. Am. Chem. Soc. 130, 4057–4068.
15. Pellissier, H. (2006) Use of chiral sulfoxides in asymmetric synthesis. Tetrahedron 62, 5559–5601.
16. Fernández, I. and N. Khar (2003) Recent developments in the synthesis and utilization of chiral sulfoxides. Chem. Rev. 103, 3651–3705.
17. Legros, J., J. R. Dehli and C. Bolm (2005) Applications of catalytic asymmetric sulfoxide oxidations to the syntheses of biologically active sulfoxides. Adv. Synth. Catal. 347, 19–31.
18. Bentley, R. (2005) Role of sulfur chirality in the chemical processes of biology. Chem. Soc. Rev. 34, 609–624.
19. Shin, J. M. Y., M. Cho and G. Sachs (2004) Chemistry of covalent inhibition of the gastric (H+–K+)-ATPase by proton pump inhibitors. J. Am. Chem. Soc. 126, 7800–7811.
20. Ganesan, M., V. K. Sivasubramanian, S. Rajagopal and R. Ramaraj (2004) Electron transfer reactions of organic sulfoxides with photochemically generated ruthenium(III)–polypyrrolid complexes. Tetrahedron 60, 1921–1929.
21. Bacciocchi, E., T. Del Giacco, M. F. Gerini and O. Lanzalunga (2006) Aryl sulfoxide radical cations. generation, spectral properties, and theoretical calculations. J. Phys. Chem. A 110, 9940–9948.
22. Bacciocchi, E., D. Intini, A. Piromattei, C. Rol and R. Ruzziioni (1989) Product and kinetic study of the oxidation of thioethers by cerium(IV) ammonium nitrate in acetic acid. Gazz. Chim. Ital. 119, 649–652.
23. Bacciocchi, E., O. Lanzalunga, A. Lapi and L. Magini (2009) Stereochrome of the C–S bond cleavage in cis-2-methylcyclopropyl phenyl sulfoxide radical cation. J. Org. Chem. 74, 1805–1808.
24. Bacciocchi, E., T. Del Giacco, O. Lanzalunga, P. Mencarelli and B. Procacci (2008) Photosensitized oxidation of alkyl phenyl sulfoxides. C–S Bond cleavage in alkyl phenyl sulfoxide radical cations. J. Org. Chem. 73, 5675–5682.
25. Del Giacco, T., O. Lanzalunga, A. Lapi, M. Mazzonna and P. Mencarelli (2015) Photosensitized oxidation of aryl benzyl sulfoxides. Evidence for nucleophilic assistance to the C–S bond cleavage of aryl benzyl sulfoxide radical cations. J. Org. Chem. 80, 2310–2318.
26. Bacciocchi, E., O. Lanzalunga, S. Malandracco, M. Ioele and S. Steenkens (1996) Oxidation of sulfides by peroxydases. Involvement of radical cations and the rate of the oxygen rebound step. J. Am. Chem. Soc. 118, 8973–8974.
27. Bacciocchi, E., M. Biett and O. Lanzalunga (2000) Mechanistic aspects of β-bond-cleavage reactions of aromatic radical cations. Acc. Chem. Res. 33, 243–251.
28. Barbieri, A., R. De Carlo Chimenti, T. Del Giacco, S. Di Stefano, O. Lanzalunga, A. Lapi, M. Mazzonna, G. Olivero and M. Salamone (2016) Oxidation of aryl diphenylmethyl sulfides promoted by a
nonheme iron(IV)-oxo complex: evidence for an electron transfer–oxygen transfer mechanism. *J. Org. Chem.* **81**, 2513–2520.

29. Barbiere, A., T. Del Giacco, S. Di Stefano, O. Lanzalunga, A. Lapi, M. Mazzonna and G. Olivo (2016) Electron transfer mechanism in the oxidation of aryl 1-methyl-1-phenylethyl sulfides promoted by nonheme iron(IV)–oxygen complexes: the role of the oxygen rebound process. *J. Org. Chem.* **81**, 12382–12387.

30. Barbiere, A., S. Di Stefano, O. Lanzalunga, A. Lapi, M. Mazzonna and G. Olivo (2017) Role of electron transfer processes in the oxidation of aryl sulfides catalyzed by nonheme iron complexes. *Phosphorus, Sulfur, Silicon Related Elements* **192**, 241–244.

31. Del Giacco, T., O. Lanzalunga, M. Mazzonna and P. Mencarelli (2012) Structural and solvent effects on the C-S bond cleavage in aryl triphenylmethyl sulfide radical cations. *J. Org. Chem.* **77**, 1843–1852.

32. Baciocchi, E., M. Bettoni, T. Del Giacco, O. Lanzalunga, M. Mazzonna and P. Mencarelli (2011) Structure and C-S bond cleavage in aryl 1-methyl-1-arylethyl sulfide radical cations. *J. Org. Chem.* **76**, 573–582.

33. Baciocchi, E., T. Del Giacco, P. Giombolini and O. Lanzalunga (2006) C-S Bond cleavage in the sensitized photooxygenation of t-alkyl phenyl sulfides. The role of superoxide anion. *Tetrahedron* **62**, 6566–6573.

34. Baciocchi, E., M. F. Gerini, T. Del Giacco and O. Lanzalunga (2006) Rates of C-S Bond cleavage in t-alkyl phenyl sulfide radical cations. *Org. Lett.* **8**, 641–644.

35. Baciocchi, E., T. Del Giacco, F. Elisei, M. F. Gerini, A. Lapi, P. Liberilli and B. Uzzoli (2004) Steady-state and laser flash photolysis study of the carbon-carbon bond fragmentation reactions of 2-aryl sulfanyl alcohol radical cations. *J. Org. Chem.* **69**, 8323–8330.

36. J. L. Rice and J. K. Kochi (eds.) (1973) *Free Radicals*. John Wiley & sons, New York.

37. Kitaguchi, H., K. Ohkubo, S. Ogo and S. Fukuzumi (2006) Electron-transfer oxidation properties of unsaturated fatty acids and mechanistic insight into lipooxigenases. *J. Phys. Chem. A* **110**, 1718–1725.

38. Kato, S., J. Nakata and E. Imoto (1971) Electrochemical reduction and oxidation of aza-heteroaromatic compounds. IV. stabilities of neutral free radicals: role of structural and medium effects. *Bull. Chem. Soc. Jpn.* **44**, 1928–1933.

39. Ramesh, M. and J.-F. Biellmann (1988) Effect of the Base on the Stereoselectivity of the Reaction of a Carbanion with an Aldehyde. *Synth. Commun.* **18**, 333–335.

40. Kingsbury, C. A. (1972) Asymmetric synthesis of diastereomeric hydroxy sulfides, sulfoxides, and sulfones by condensation and oxidation reactions. *J. Org. Chem.* **37**, 102–106.

41. Zhou, S.-F., P. Xiangjiu, Z.-H. Zhou, A. Shoberu and J.-P. Zou (2015) Air oxidative radical hydroxy sulfuration of styrenes leading to β-hydroxy sulfoxides. *J. Org. Chem.* **80**, 3682–3687.

42. Watanabe, M., S. Nakamori, H. Hasegawa, K. Shirai and T. Kumanoto (1981) New synthetic route for the preparation of 4-phenylthio-4-butanolide derivatives by the use of the Pummerer rearrangement. *Bull. Chem. Soc. Jpn.* **54**, 817–821.

43. Colonna, S., V. Pirotoni, F. Zambianchi, G. Ottolina, N. Gaggero and G. Celentano (2007) Diastereoselective synthesis of β-hydroxy sulfides: enzymatic and biomimetic approaches. *Eur. J. Org. Chem.* 363–368.

44. Marples, B. A., C. G. Saint and J. R. Traynor (1986) Regiochemistry of nucleophilic opening of β-substituted styrene oxides with thiolate anions: model experiments in the synthesis of leukotriene analogues. *J. Chem. Soc., Perkin Trans. I*, 567–574.

45. Ludwig, G., T. Rüffer, A. Hoppe, T. Walther, H. Lang, S. G. Ebbinghaeus and D. Steinborn (2015) Lithiated sulfides: α-sulfanyl functionalized carbanions. *Dalton Trans.* **44**, 5323–5330.

46. Cavattoni, T., T. Del Giacco, O. Lanzalunga, M. Mazzonna and P. Mencarelli (2013) Structural effects on the C-S bond cleavage in aryl tert-butyl sulfoxide radical cations. *J. Org. Chem.* **78**, 4886–4894.

47. Nichols, M. A., A. T. McPhail and E. M. Arnett (1991) Chelation of 2-substituted 1-lithoxides: structural and energetic factors of relevance to synthetic organic chemistry. *J. Am. Chem. Soc.* **113**, 6222–6233.

48. Hassner, A. and R. H. Reuss (1974) Chemistry of carbanions. VIII. Pathways in the base-catalyzed decomposition of cyclic N-nitrosocarbamates. *J. Org. Chem.* **39**, 553–560.

49. Kelly, C. B., K. M. Lambert, M. A. Mercadante, J. M. Ovian, W. F. Bailey and N. E. Leadbeater (2015) Access to nitriles from aldehydes mediated by an oxoammonium salt. *Angew. Chem. Int. Ed.* **54**, 4241–4245.

50. Kavarnos, G. J. and N. J. Turro (1986) Photosensitization by reversible electron transfer: theories, experimental evidence, and examples. *Chem. Rev.* **86**, 401–449.

51. Murov, S. L. (1973) *Handbook of Photochemistry*. M. Dekker, New York.

52. Dockery, K. P., J. P. Dinncocenzo, S. Farid, J. L. Goodman, I. R. Gould and W. P. Todd (1997) Nucleophile-assisted cleavage of benzyltrialkylsilane cation radicals. *J. Am. Chem. Soc.* **119**, 1876–1883.

53. Alamone, M. and M. Bietti (2015) Tuning reactivity and selectivity of nucleophilic opening of epoxides: a selective synthesis of substituted benzylic carbanions. *Eur. J. Org. Chem.* **2015**, 6222–6233.

54. Rau, B. C. and U. Jana (1998) Indium(III) chloride-promoted rearrangement of epoxides: a selective synthesis of substituted benzylic aldehydes and ketones. *J. Org. Chem.* **63**, 8212–8216.

55. Okubo, K., K. Suga, K. Morikawa and S. Fukuzumi (2003) Selective oxygenation of ring-substituted toluenes with electron-donating and -withdrawing substituents by molecular oxygen via photoinduced electron transfer. *J. Am. Chem. Soc.* **125**, 12850–12859.

56. Kishore, K. and K. D. Asmus (1989) Radical cations from one-electron oxidation of aliphatic sulfoxides in aqueous solution. A radiation chemical study. *J. Chem. Soc. Perkin Trans 2*, 2079–2088.