Visible light photooxidation of nitrate: the dawn of a nocturnal radical†

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Highly oxidizing nitrate radicals (NO3•) are easily accessed from readily available nitrate salts by visible light photoredox catalysis using a purely organic dye as the catalyst and oxygen as the terminal oxidant. The interaction of the excited catalyst and nitrate anions was studied by spectroscopic methods to elucidate the mechanism, and the method was applied to the NO3• induced oxidation of alkenes and alcohols.

The nitrate radical (NO3•) is the most important nocturnal free radical oxidant in the troposphere and thus accounts for the majority of the oxidative reactions at night-time.1 In the atmosphere NO3• oxidizes a broad scope of volatile organic species including alkenes,2,3 alcohols,4,5 terpenes,1 esters,6 and sulfides.1 It is a highly reactive and chemically versatile O-centered radical7 with an oxidation potential of +2.00 V (vs. SCE in MeCN).8 Apart from electron transfer (ET),9,10 NO3• also reacts by addition to π systems1,11 and by hydrogen atom abstraction (HAT).8,12,13 Overall, the reactivity of NO3• with organic molecules can be seen in between that of hydroxyl radicals (OH•) and sulfate radical anions (SO4•−).14

Despite its high chemical versatility, it is surprising that only limited synthetic applications of NO3• are available so far. Shono reported the addition of electrochemically generated NO3• to alkenes.11 The reaction of NO3• with cyclic alkenes and alkynones was employed to obtain cis-fused bicyclic ketones in self-terminating oxidative radical cyclizations.15,16 This concept was later extended to alkylene ethers yielding tetrasubstituted tetrahydrofurans.17,18 One reason for the limited use of NO3• as a reagent in organic transformations is its rather difficult accessibility. Common methods for NO3• generation on preparative scale in solution are the reaction of nitrogen dioxide and ozone,1,19 electrooxidation of nitrate anions11 or the photolysis of (NH4)2Ce(NO3)6 (CAN) with UV light (λ = 350 nm).14,20 However, the use of toxic gases, high electrode potentials,8 or UV irradiation are so far limiting the applications and lead to undesired side reactions.

We were pleased to observe that, upon excitation of the organic photocatalyst 9-mesityl-10-methylacridinium perchlorate (1) with blue light, oxidation of nitrate anions to NO3•, readily occurs (Scheme 1), thus providing a convenient access to NO3• on a preparative scale. 9-Mesityl-10-methylacridinium perchlorate (1) was chosen, because it is known to have a strong oxidizing capacity in the excited state.21,22 To the best of our knowledge, this is the first visible light mediated generation of nitrate radicals.

In order to elucidate the mechanism of the NO3• formation, we monitored the generation of reduced catalyst Acr•-Mes in the presence of LiNO3 upon continuous irradiation of a 5 μM solution of Acr•-Mes (1) in MeCN with 455 nm light under

![Scheme 1. Proposed mechanism of visible light mediated generation of NO3• via photocatalytic oxidation by Acr•-Mes (1).](image_url)
anerobic conditions. The differential absorption spectrum shows the appearance of Acr\(^+\)-Mes with a maximum at 520 nm\(^{21,23}\) after irradiation for 120 s and 240 s. (see ESI, Fig. S6) This observation suggests a direct oxidation of NO\(_3^-\) by the excited catalyst thus demonstrating that NO\(_3^-\) can act as an electron donor to the excited catalyst. The reduced catalyst Acr\(^-\)-Mes is stable under argon, however, the signal vanishes completely after aeration of the reaction mixture due to reoxidation of Acr\(^+\)-Mes to the ground state catalyst Acr\(^-\)-Mes by oxygen (see Scheme 1).\(^{24}\) The negative signal at \(\lambda < 460\) nm in the differential absorption spectrum is caused mainly by the decrease of the ground state absorption of Acr\(^-\)-Mes as a result of Acr\(^+\)-Mes formation and partial photo-bleaching of Acr\(^+\)-Mes.\(^{2}\) The long-lived triplet state with a microsecond lifetime is generally discussed as the reactive state in most oxidative reactions.\(^{25,26}\) The exact nature of this state is controversial and could be both a CT\(^\circ\) state with an oxidation potential of +1.88 V vs. SCE, as reported by Fukuzumi\(^{25}\) or a locally excited triplet state, LE\(^T\), with an oxidation potential of +1.45 V vs. SCE as reported by Verhoeven.\(^{26}\) However, neither would have the oxidative capacity to oxidize NO\(_3^-\). Recent detailed mechanistic investigations by the group of Nicewicz revealed that for substrates with oxidation potentials exceeding +1.88 V (vs. SCE), a reaction should occur out of the short-lived excited singlet state (mainly CT\(^\circ\)) which has an estimated oxidation potential of 2.08 V (Scheme 1).\(^{23}\)

Since both singlet states are fluorescent (\(\phi_F \approx 8\%\)), whereas the triplet states do not emit,\(^{23}\) we performed fluorescence quenching experiments to explore the nature of the reactive state involved in NO\(_3^-\) oxidation. A clear quenching of the fluorescence by LiNO\(_3\) confirms that oxidation of NO\(_3^-\) occurs from the singlet excited state of 1 (see ESI, Fig. S6). Moreover, laser flash photolysis experiments confirmed that no interaction of the long lived triplet state and NO\(_3^-\) can be observed (Fig. S8 in the ESI). Based on these findings, we suggest that the reaction proceeds via a singlet excited state as depicted in Scheme 1.

Having demonstrated the pathway for photocatalytic NO\(_3^-\) generation, we selected the well-studied reaction of NO\(_3^-\) with diphenylacetylene (2) yielding benzin (3) and benzophenone (4) to explore the synthetic application of this new method and to compare it with the previously reported methods. The results are compiled in Table 1. Under photocatalytic conditions using 5 mol% of Acr\(^-\)-Mes (1), 0.25 mmol of alkyne 2 and 2 eq. of LiNO\(_3\), diketone 3 and ketone 4 were obtained after 2 h of irradiation with blue light (\(\lambda = 455\) nm) with yields comparable to previous methods.\(^{27}\) When oxygen was replaced by ammonium persulfate as the electron acceptor in a degassed system, the yield and product ratio were not changed significantly (entry 5). This shows that potential interfering reactions by singlet oxygen could be excluded. In the absence of light or catalyst no reaction occurred (entries 7 and 9). However, small amounts of diketone 3 were formed in the direct reaction of 2 with the excited catalyst in the absence of nitrate ions (entry 8).

According to computational studies, the mechanism for the NO\(_3^-\) induced oxidation of diphenylacetylene suggests formation of diketone 3 and benzophenone (4) through competing pathways in the initial vinyl radical adduct 5 (Scheme 2). While diketone 3 results from a 5-\(\text{endo}\) cyclization, followed by loss of NO\(_2\), the key-step in the formation of benzophenone (4) is \(\gamma\)-fragmentation with elimination of NO\(_3^+\), and subsequent Wolff-rearrangement of the carbene intermediate 7 followed by oxidative decarboxylation.\(^{27}\)

Next, we applied the photocatalytic NO\(_3^-\) formation to the synthesis of tetrasubstituted tetrahydrofurans, which proceeds \(\textit{via}\) a self-terminating radical cascade that is initiated by NO\(_3^-\) addition to the triple bond in alkyne 9. The reaction was described previously using either anodic oxidation of lithium nitrate or CAN photolysis.\(^{17,18}\) The starting material 9 (Scheme 3) contains an aliphatic alkyne, which is more difficult to oxidize compared to 2 and thus decreases the background reaction that is caused by direct oxidation of 9 by the photocatalyst. The reaction of 9b with 2 eq. of LiNO\(_3\) and 5 mol% I gave the anticipated product 10b in a yield of 37% (67% based on conversion), with 45% of the starting material 9b being recovered. Methyl ether 9a gave lower yields and

<table>
<thead>
<tr>
<th>Entry</th>
<th>Conditions</th>
<th>Yield(^a) 3 + 4 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5 mol% 1, air</td>
<td>50 (30 + 20)</td>
</tr>
<tr>
<td>2</td>
<td>5 mol% 1, O(_2)</td>
<td>55 (31 + 24)</td>
</tr>
<tr>
<td>3</td>
<td>NaNO(_3)</td>
<td>41 (27 + 15)</td>
</tr>
<tr>
<td>4</td>
<td>10 mol% 1</td>
<td>38 (24 + 14)</td>
</tr>
<tr>
<td>5</td>
<td>[NH(_4)](_2)S(_2)O(_8), N(_2) atmosphere</td>
<td>46 (27 + 19)</td>
</tr>
<tr>
<td>6</td>
<td>DCIM</td>
<td>52 (32 + 20)</td>
</tr>
<tr>
<td>7</td>
<td>Without light</td>
<td>0</td>
</tr>
<tr>
<td>8</td>
<td>Without NO(_3^-)</td>
<td>13 (3 only)</td>
</tr>
<tr>
<td>9</td>
<td>Without 1</td>
<td>0</td>
</tr>
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</table>

\(a\) Reactions were carried out using diphenylacetylene (2, 0.25 mmol) and the respective amount of 9-mesityl-10-methylacridinium perchlorate (1) in 1 mL of MeCN unless otherwise noted with an irradiation time of 2 h.

\(b\) Quantitative GC yields using acetophenone as internal standard.
an incomplete conversion, which can be rationalized by a non-regioselective addition of NO$_3^+$ to both ends of the alkyne, which was explored in the catalytic oxidation of non-activated alcohols. In this reaction, NO$_3^+$ acts as a redox mediator, which is regenerated during the catalytic cycle, according to the mechanism in Scheme 4. Initial HAT from the alcohol carbon atom by NO$_3^+$ leads to the regeneration of NO$_3$ as nitric acid and formation of radical 12. The latter is subsequently oxidized by either NO$_3^+$ or oxygen to give cationic intermediate 13, which deprotonates to yield ketone 14. The mechanism is similar to the indirect anodic oxidation of alcohols by nitrate. Donaldson and Styler reported the enhanced gas phase oxidation of propanol under UV irradiation using TiO$_2$ co-embedded with KNO$_3$. The finding was explained by formation of NO$_3^+$ and its ability to abstract hydrogen atoms from the alcohol carbon atom.

The reaction was explored using tert-butyl cyclohexanol (11a) and the results are compiled in Scheme 5. To our delight, oxidation into the corresponding ketone 14a occurred upon irradiation with blue light in the presence of LiNO$_3$ using 5 mol% of 1 in acetonitrile. No reaction was observed in the absence of nitrate, which clearly confirms the role of NO$_3^+$ in this reaction. Stepwise reduction of the amount of LiNO$_3$ from 2 eq. to 20 mol% did not affect the outcome, showing that NO$_3^+$ can act as mediator in this reaction (Scheme 5). An acidification of the solution due to formation of nitric acid was observed, but no apparent influence on the reaction or the stability of the catalyst was found.

The scope of this method was explored towards other non-activated alcohols and electron deficient benzyl alcohols.

![Scheme 4](image)

**Scheme 4** General mechanism of the nitrate mediated alcohol oxidation via initial hydrogen abstraction followed by oxidation and loss of a proton.

![Scheme 5](image)

**Scheme 5** Experimental conditions and results for the NO$_3^+$ mediated oxidation of alcohols.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alcohol</th>
<th>Product</th>
<th>Yield product</th>
<th>Recovered starting material</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11a</td>
<td>14a</td>
<td>45 (79)</td>
<td>44</td>
</tr>
<tr>
<td>2</td>
<td>11b</td>
<td>14b</td>
<td>42 (95)</td>
<td>56</td>
</tr>
<tr>
<td>3</td>
<td>11c</td>
<td>14c</td>
<td>40 (40)</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>11d</td>
<td>14d</td>
<td>55 (100)</td>
<td>45</td>
</tr>
<tr>
<td>5</td>
<td>11e</td>
<td>14e</td>
<td>— d</td>
<td>— d</td>
</tr>
<tr>
<td>6</td>
<td>11f</td>
<td>14f</td>
<td>16 (20)</td>
<td>17</td>
</tr>
</tbody>
</table>

*All reactions were carried out by two sequential additions of 5 mol% of 1 in order to counteract the loss of catalytic activity caused by degradation of the catalyst. The reactions proceed with good selectivity (see Table 2, entries 1, 2, 4), but the conversion was incomplete and unreacted starting material was recovered. Aliphatic (entries 1–3) and benzylic alcohols (entries 4 and 6) were converted.*

In conclusion, we described a new and simple access to highly reactive nitrate radicals using visible light photocatalysis with an organic dye as the photoredox catalyst. This method avoids the use of toxic compounds, or high electrochemical potentials and is, to the best of our knowledge, the first method yielding NO$_3^+$ in a catalytic process using visible light. We verified the formation of nitrate radicals by observation of the reduced catalyst Acryl$\cdot$Mes and showed that the mechanism is proceeding via the singlet excited state of the catalyst. By investigating the addition to aromatic alkyynes, a previously well studied model reaction of NO$_3^+$, we showed that the photocatalytic procedure is as efficient as the previously employed methods.

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Notes and references

‡ After aeration the ground state absorption of Acr+-Mes cannot be fully recovered (see ESI†).
§ For the mechanism of this reaction see ESI†.
¶ The addition of different bases (LiNO₃, LiOAc, pyridine, lutidine) did not influence the outcome of the reaction or the stability of the catalyst.

Based on the assumption that both the initial hydrogen abstraction and the oxidation of 12 are done by nitrate radicals.