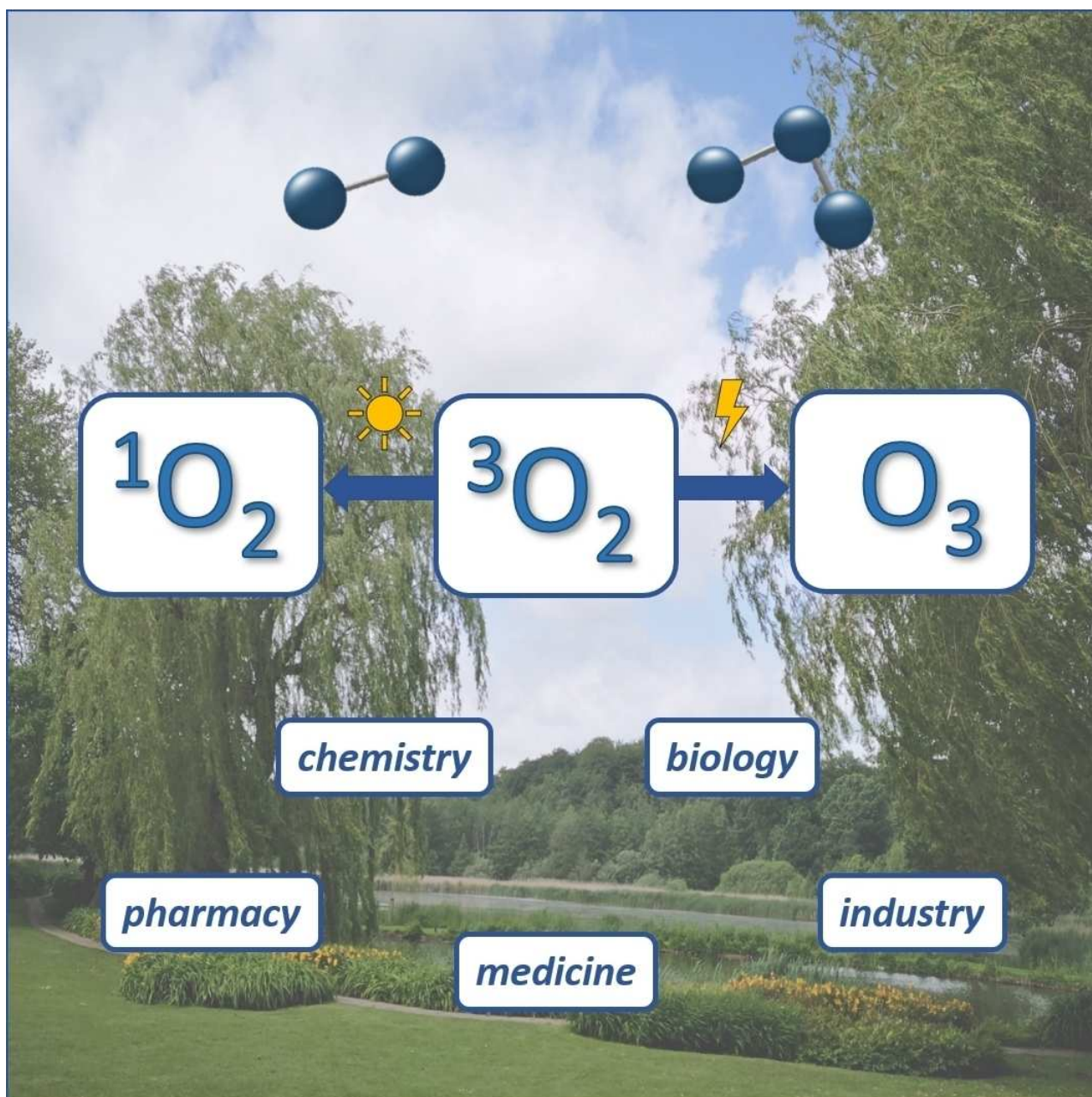


# The Diverse Modes of Oxygen Reactivity in Life & Chemistry

Robin Stuhr,<sup>[a]</sup> Patrick Bayer,<sup>[b]</sup> and Axel Jacobi von Wangelin<sup>\*[a]</sup>



Oxygen is a molecule of utmost importance in our lives. Beside its vital role for the respiration and sustaining of organisms, oxygen is involved in numerous chemical and physical processes. Upon combination of the different forms of molecular oxygen species with various activation modes, substrates, and reaction conditions an extremely wide chemical space can

be covered that enables rich applications of diverse oxygenation processes. This Review provides an instructive overview of the individual properties and reactivities of oxygen species and illustrates their importance in nature, everyday life, and in the context of chemical synthesis.

## 1. Introduction

Oxygen (atomic number 8) is the most abundant element by mass in the Earth's crust, hydrosphere, and biosphere. Bonded oxygen is a major component of minerals (e.g., silicates, oxides, carbonates, sulfates, phosphates, nitrates, etc.), water, and biomolecules (carbohydrates, lignin, proteins, fats) (see Figure 1). Oxygenated species constitute the key components of all global biogeochemical cycles (e.g., carbon, nitrogen, phosphorus, sulfur).<sup>[1]</sup> Despite the undeniable importance of all these compounds, this Review focuses on elemental oxygen, the most widely dispersed and mobile member of the oxygen family tree.

Elemental oxygen exists in different allotropes, the most important species being molecular dioxygen O<sub>2</sub> (hereafter also referred to as oxygen) that makes up 21% of the Earth's atmosphere. It was first recognized as a chemical element in 1774 and given the name *oxygène* (from the Greek *oxys*: "acid producer") in 1777 by Antoine Lavoisier. Despite its simple structure, typically but wrongly drawn O=O, it exhibits rather unusual properties regarding its magnetic behavior, energy-transfer abilities, and chemical reactivities toward various compounds.

Sixteen electrons are filled into the molecular orbitals of O<sub>2</sub> according to the Aufbau principle (orbitals are filled starting at the lowest possible energy levels), the Pauli exclusion principle (no two electrons can have the same set of quantum numbers), and Hund's rule (which states that energy is lowest when degenerate orbitals are occupied by two electrons singly and with the same spin before, for the second-lowest energetic state, they are filled in one orbital as a pair). Three electronic configurations of molecular oxygen are depicted in Figure 2: the biradical triplet ground state  $^3\Sigma_g^-$ , the first excited singlet state  $^1\Delta_g$ , and the second excited singlet state  $^1\Sigma_g^+$ . Unlike the vast majority of molecules we know, O<sub>2</sub> has a paramagnetic triplet ground state (called "triplet oxygen" and denoted  $^3O_2$ ).

The ground state ( $^3\Sigma_g^-$ ) has two unpaired electrons, a phenomenon that typically encourages other radicals or biradicals to stabilize themselves by forming bonds to each other, and to neighboring oxygen or hydrogen atoms (Figure 2, top).<sup>[2]</sup> In contrast, the lowest-energy excited electronic configuration of oxygen is a singlet spin state (commonly called "singlet oxygen" and denoted  $^1O_2$ ) featuring a significantly different but no less rich chemistry, which is characterized by several rather selective transformations.<sup>[3]</sup> Distinct reactivities are known for  $^3O_2$  and  $^1O_2$ , as well as the trioxygen allotrope ozone (O<sub>3</sub>) (Figure 2, center).<sup>[4–6]</sup> The individual reactivity profiles include significantly different rates of reactions with several chemical compounds and even diverging reactivities with identical substrates (hydrocarbons, radical species, metals, furans, etc.). An illustrative example is the reaction of oxygen species with furan derivatives: Ozone effects the oxidative cleavage of the C=C bonds; cycloaddition with the diene component operates with  $^1O_2$ ; oxidative homo-coupling to a furan dimer is observed when reacting furans with aerial  $^3O_2$  in the presence of a metal catalyst (Figure 2, bottom).<sup>[7–9]</sup> Further species such as the high-energy second excited singlet oxygen and allotropes like the oxygen atom, O<sub>4</sub>, or O<sub>8</sub> are only short-lived or require special conditions and therefore have little applications.<sup>[10–12]</sup> This Review is intended to provide exemplary insights into the nature, properties, chemical reactivities, and technical applications of the three most prominent molecular oxygen species  $^3O_2$ , O<sub>3</sub>, and  $^1O_2$ . Major emphasis is placed on diverse applications from various fields, important aspects of modern research, and instructive experiments for education purposes. The short-lived allotropes and the so-called "reactive oxygen species" (ROS, e.g., H<sub>2</sub>O<sub>2</sub>, O<sub>2</sub><sup>•-</sup>, OOH) will not be covered in this Review.<sup>[13,14]</sup>

## 2. Triplet Oxygen ( $^3O_2$ )

### 2.1. General

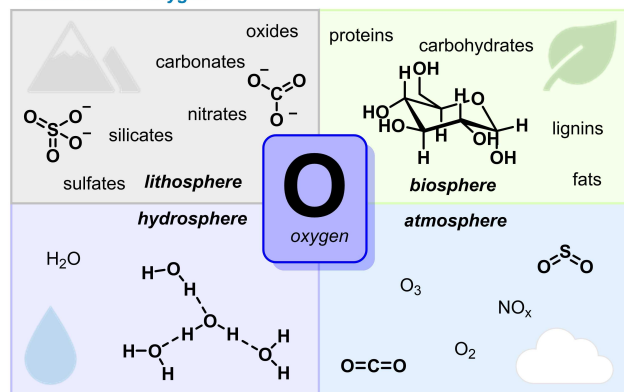
Aerial oxygen is a color- and odorless gas at standard conditions; in liquid (b.p.: –183 °C) and solid state (m.p.: –218 °C) it appears blueish.<sup>[1]</sup> Triplet oxygen is especially reactive in contact with other radicals while it is kinetically persistent toward reactions with most other compounds. Triplet oxygen does not (readily) abstract hydrogen atoms to form HOO• under reaction conditions where the more reactive peroxy radicals ROO• easily engage in such H atom transfer (HAT). This is due to the very large resonance stabilization energy of  $^3O_2$  that effects strong  $\pi$ -bonding and can be explained by valence bond (VB) and molecular orbital (MO)

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## – Occurrence of oxygen



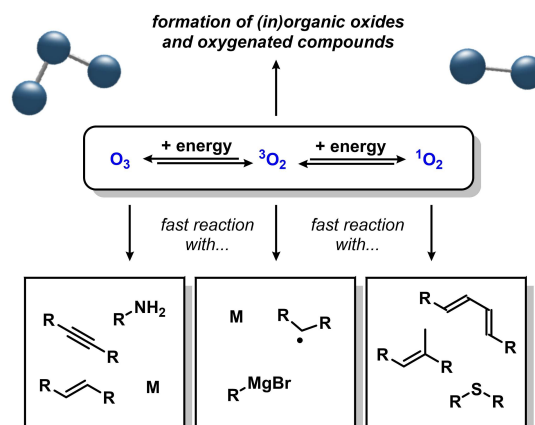
**Figure 1.** Occurrence of oxygen in the lithosphere, biosphere, hydrosphere, and atmosphere.

theories.<sup>[2]</sup> It is important to note that  $^3\text{O}_2$ , however, has an exothermic energy balance in reactions with almost every compound or element on the surface of our planet. In that sense, oxygen is an energetic molecule that is only held back from rapid reactions by high activation barriers (i.e., at best it reacts with very slow rates). The hydrogen balloon exploding in a chemistry class does not go off until activation energy in form of a spark is present; likewise, paper does not ignite spontaneously in air until it reaches a temperature of about 230 °C. The combustion of organic compounds occurs via a series of exothermic radical pathways.<sup>[15,16]</sup> A fine dispersion of combustible compounds in  $\text{O}_2/\text{air}$  (flour, coal dust, organic solvent vapors, etc.) can form explosive mixtures due to the very large surface area. Flames burn stronger in pure oxygen than in air; a fact that is used to detect oxygen (or other oxidizing gases) by the glowing splint test in school labs. Therefore, reactions with pure oxygen have to be handled with greatest care. Even greater reactivities are observed in liquid oxygen: for example, the mixture of solid lithium hydride and liquid oxygen is an

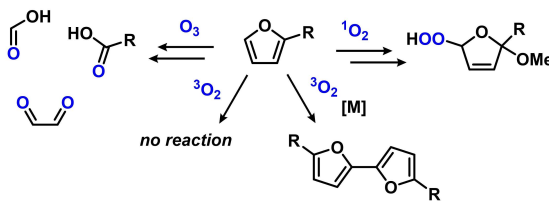
– Electronic configurations of  $\text{O}_2$ 

MO	$\text{O}_2(^3\Sigma_g^-)$	$\text{O}_2(^1\Delta_g)$	$\text{O}_2(^1\Sigma_g^+)$	$E_{\text{rel}} / \text{kJ mol}^{-1}$
$3\sigma_u$				
$1\pi_u$	$\uparrow \uparrow$	$\uparrow \downarrow$	$\uparrow \downarrow$	157 $\text{O}_2(^1\Sigma_g^+)$
$1\pi_g$	$\uparrow \downarrow \uparrow \downarrow$	$\uparrow \downarrow \uparrow \downarrow$	$\uparrow \downarrow \uparrow \downarrow$	96 $\text{O}_2(^1\Delta_g)$
$3\sigma_g$	$\uparrow \downarrow$	$\uparrow \downarrow$	$\uparrow \downarrow$	0 $\text{O}_2(^3\Sigma_g^-)$

## – Elemental oxygen species



## – Diverging reactivities



**Figure 2.** Molecular orbital (MO) occupation of ground and excited states of  $\text{O}_2$ . MOs are sorted by energy in ascending order;  $(1\sigma_g)^2(1\sigma_u)^2(2\sigma_g)^2(2\sigma_u)^2$  were omitted for simplicity (top). Reactivity of elemental oxygen species (middle). Distinct reaction pathways of oxygen species with furans (bottom).



Robin Stuhr is a native of Northern Germany. He undertook Chemistry studies at the Universities of Hamburg and San Sebastián (Spain). As Kekulé doctoral fellow of the Fonds der Chemischen Industrie, Robin currently investigates photoredox catalysis and biomass valorization.



Patrick Bayer hails from the German–Austrian border region. He studied Chemistry at the University of Regensburg and obtained his Ph.D. from the University of Hamburg on photooxygenation of olefins. Patrick has recently joined Thermo Fisher at their Linz site.

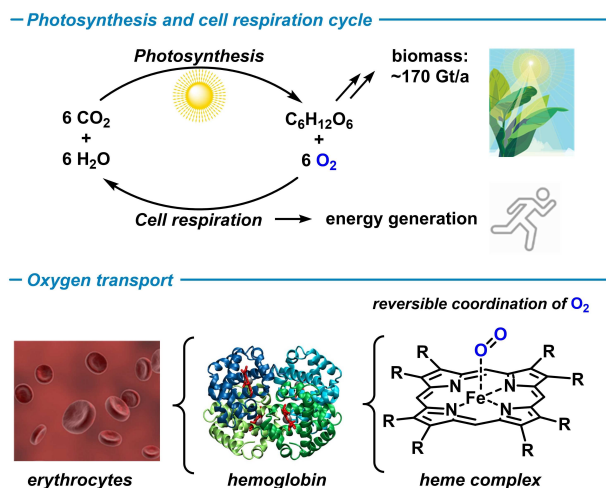


Axel Jacobi von Wangelin was born in Berlin and saw the graffiti-free side of the wall collapsing. He later enjoyed vibrant college lives in Erlangen, Utah, Cardiff, Rostock, Stanford, Cologne, and Regensburg. He is Professor of Molecular Chemistry at the University of Hamburg. His groups research spans all aspects of catalysis.

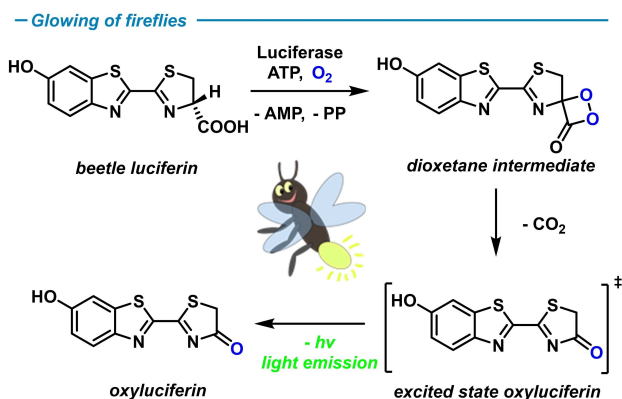
explosive of much greater power than trinitrotoluene (TNT).<sup>[17]</sup> Many rather standard chemicals, including car fuels or other hydrocarbons, become very powerful explosives when treated with liquid  $^3\text{O}_2$ .<sup>[18]</sup>

## 2.2. Nature

The oxygen content of the Earth's atmosphere originates from the oxidation of water via photosynthesis processes over the course of millions of years. Today, approximately 170 Gt of biomass are formed by photosynthesis each year. All higher life forms on earth are directly dependent on the constant availability of oxygen. The reduction of  $^3\text{O}_2$  to water is a key step of the aerobic respiration and responsible for the generation of adenosine triphosphate (ATP), the cellular "energy currency" that drives many reactions in living cells. The oxidation of iron to rust is a process that is known to everyone. A closely related reaction of oxygen with an iron atom is the transport of oxygen into the cells of almost all vertebrates,



**Figure 3.** Photosynthesis and cell respiration cycle (top), oxygen transport in the blood (bottom), structure of hemoglobin. Reprinted from Ref. [20]. Copyright (2021), with permission of Springer Nature.



**Figure 4.** Role of oxygen in the signaling mechanism of fireflies.

which operates via the reversible binding to the iron-containing protein hemoglobin in red blood cells (Figure 3).<sup>[19]</sup>

Furthermore, oxygen is an important substrate in many enzyme-catalyzed biosynthetic pathways that convert molecules for energy and heat release, digestion, detoxification, signaling pathways, and so on. Oxidases, monooxygenases, and dioxygenases utilize  $^3\text{O}_2$  as oxidant and source of incorporation of one or two oxygen atoms into biomolecules, respectively. Among other oxidative mechanism, enzymatic hydroxylations and epoxidations are especially frequent.<sup>[21,22]</sup> A rather special application of  $^3\text{O}_2$  is its role in the glowing of fireflies (Figure 4). The enzyme luciferase catalyzes the reaction of molecular oxygen with luciferin, forming an unstable four-membered ring, the dioxetane intermediate. Elimination of  $\text{CO}_2$  gives oxyluciferin in a thermally excited state. The transition into the ground state is accompanied by the emission of a photon. As a result, the firefly glows. Similar oxygen-dependent bioluminescence processes can be found, among others, in bacteria, algae, jellyfishes, and squids.<sup>[23]</sup>

## 2.3. Technologies

From an industrial perspective, pure oxygen is a low-price commodity that is produced directly from air. The most common procedure is liquification and subsequent distillation of air (b.p.  $\text{O}_2$ :  $-183^\circ\text{C}$ , b.p.  $\text{N}_2$ :  $-196^\circ\text{C}$ ). Another possibility is the absorption of nitrogen from a dry air stream by zeolite sieves. The electrolysis of water to generate  $\text{O}_2$  is technically possible but not profitable on larger scales due to the high consumption of electricity and metal catalyst materials. The more reactive forms of oxygen ( $^1\text{O}_2$ ,  $\text{O}_3$ ) are usually not stored but generated from  $^3\text{O}_2$  in situ or on-site.<sup>[24]</sup> The largest single consumer of  $\text{O}_2$  is the steel industry, which requires huge quantities of  $\text{O}_2$  for the oxidation of carbon and sulfur impurities to volatile  $\text{CO}_2$  and  $\text{SO}_2$  flue gases. Very minor uses of  $\text{O}_2$  are, for example, medical applications such as the mechanical ventilation of patients. Oxygen is also applied in the context of environmental remediation, for example, of contaminated water or soils. Such bioremediation processes harness the activity of aerobic microbes to remove chemical pollutants (e.g., hydrocarbons, fuels, drug remnants, fertilizers). A major limitation is the low oxygen availability in these environments. Therefore, additional oxygen is added by direct air sparging or injection of oxygen-releasing compounds to speed up renaturation efforts in polluted environments.<sup>[25–27]</sup> Wastewater treatment plants also rely on oxygen to enhance their detoxification efficiency.<sup>[28]</sup> Aqua-culturists such as fish farmers benefit from oxygen introduction into freshwater lakes and rivers by the health or size of their livestock.<sup>[29]</sup>

Oxygen, hydrogen, and their reaction product water constitute the basis of the "hydrogen economy", a hypothetical future scenario of a carbon emission-free economy (Figure 5, top). Firstly, water, a renewable resource, is electrolytically split into gaseous hydrogen and oxygen. This reaction must be powered by energy from renewable resources in order to be fully sustainable. The produced hydrogen gas can then be

## – Idealistic hydrogen economy

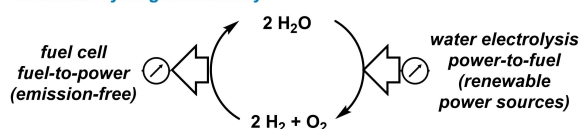
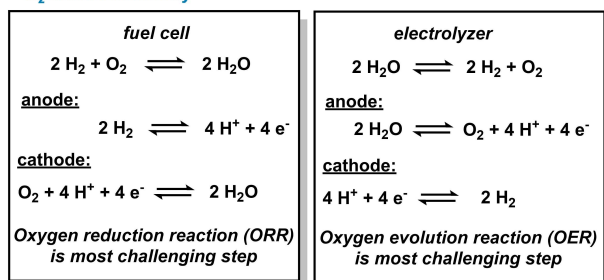
– O<sub>2</sub> electrochemistry

Figure 5. Idealistic hydrogen economy (top) and involved electrochemistry (bottom).

stored and distributed to its individual applications. There, hydrogen is oxidized or “burned” by oxygen to water in fuel cells that produce no other emissions. Both electrolysis and fuel cell reaction require advanced catalysts, whose development is a vibrant research topic.<sup>[33]</sup> In electrolysis, the oxygen evolution reaction (OER) constitutes the most challenging step due to its significant overpotential.<sup>[34,35]</sup> On the other hand, the oxygen reduction reaction (ORR) is most critical in the fuel cell operations (Figure 5, bottom). Beside metals, new research is directed at metal-free and molecular catalysts.<sup>[36–38]</sup>

Molecular oxygen is also involved in the large-scale syntheses of many inorganic (sulfuric acid, nitric acid, titanium dioxide) and organic bulk chemicals such as ethylene oxide, acrylic acid and terephthalic acid (Figure 6). Many technical applications of bulk chemical oxidations are performed as gas-phase reactions at elevated temperature and pressure in the

## – Synthesis of bulk chemicals

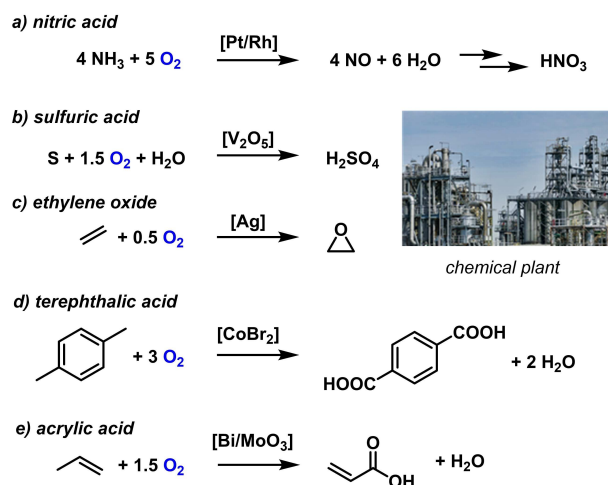


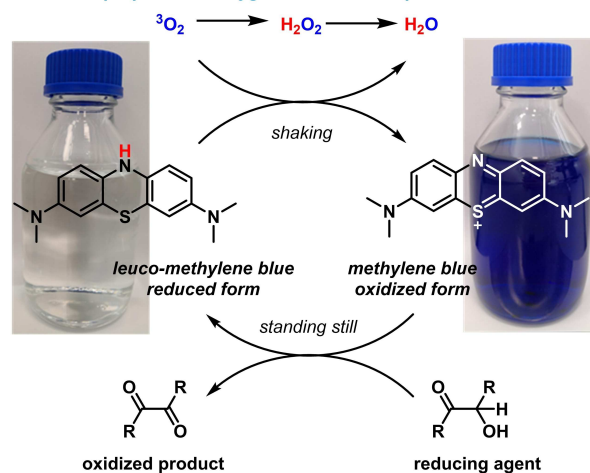
Figure 6. Oxygen in the synthesis of selected bulk chemicals.

presence of heterogenous metal(oxide) catalysts. The annual production volume of such commodity and bulk chemicals is in the multimillion-ton range.<sup>[24]</sup>

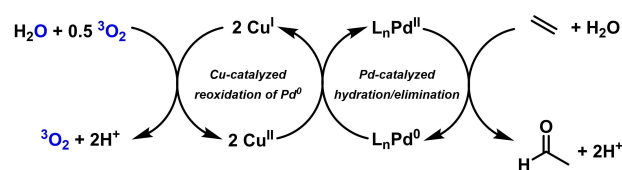
## 2.4. Synthesis

In organic synthesis, <sup>3</sup>O<sub>2</sub> is employed in diverse mechanistic settings paralleling the biological mode of oxidations: as stoichiometric oxidant or as source for the introduction of oxygen atoms into organic molecules. Triplet oxygen has a high oxidizing power; its standard potential (vs. standard hydrogen electrode, SHE) ranges from +0.401 to +1.229 V in basic to acidic aqueous media, respectively. A highly instructive visualization of the redox properties of oxygen is the blue-bottle experiment (Figure 7, top). An aqueous solution of the organic dye methylene blue and a reducing agent (e.g., glucose) is filled into a bottle. Upon standing, the dye is reduced into its

## – Oxidation properties of oxygen: blue bottle experiment



## – Wacker process: synthesis of acetaldehyde



## – Anthraquinone process: synthesis of hydrogen peroxide

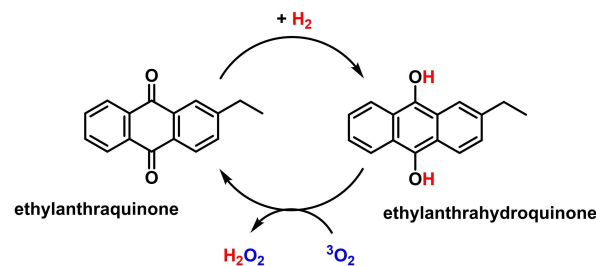


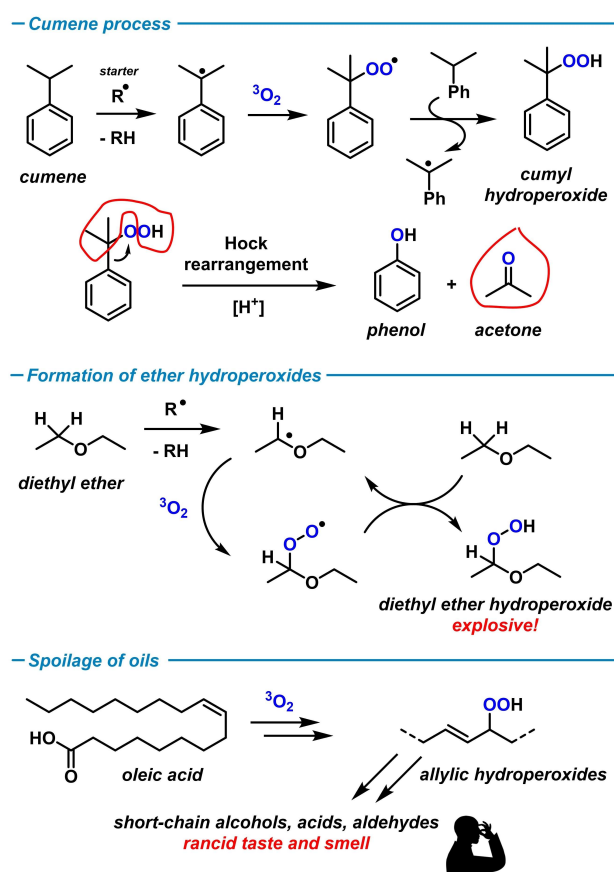
Figure 7. Applications of <sup>3</sup>O<sub>2</sub> as oxidant: Blue bottle experiment (top), Wacker process (middle), anthraquinone process (bottom).

colorless leuco-form leading to the discoloration of the solution. Shaking the bottle transfers oxygen from the gas phase into the solution; the dye is reoxidized and the blue color reappears. This redox cycle can be repeated several times until the reducing agent is fully consumed.<sup>[30]</sup>

$^3\text{O}_2$  is often employed as the stoichiometric oxidant of a reaction cascade without reacting directly with the substrate but rather with a redox mediator or catalyst. Many transition metal complexes mediate oxidation processes during which the metal undergoes net reduction. The role of  $^3\text{O}_2$  is the oxidation and regeneration of the active metal species into the original oxidation state to enable a catalytic reaction. A prominent example is the Wacker oxidation of olefins to aldehydes (Figure 7, middle). The industrial Wacker process comprises the homogenous oxidation of ethylene to acetaldehyde by a palladium(II) catalyst. During the reaction,  $\text{Pd}^{\text{II}}$  is reduced to  $\text{Pd}^0$ ; the active  $\text{Pd}^{\text{II}}$  species is regenerated by oxidation with a  $\text{Cu}^{\text{II}}$  salt. The resulting  $\text{Cu}^{\text{I}}$  is reoxidized by  $^3\text{O}_2$  to give  $\text{Cu}^{\text{II}}$ . Molecular oxygen is therefore the terminal oxidant, while the two metal salts act as catalytic redox shuttles.<sup>[31]</sup> Another technical application of oxygen redox is the  $\text{H}_2\text{O}_2$  production in the anthraquinone process (Figure 7, bottom). An organic substrate such as ethyl anthraquinone is hydrogenated by gaseous  $\text{H}_2$  to its hydroquinone form. Subsequent reaction with  $\text{O}_2$  yields hydrogen peroxide and regenerates the quinone.<sup>[32]</sup>

$^3\text{O}_2$  can act as source of oxygen atoms for the introduction into organic molecules (usually being also an oxidation process). The introduction of  $-\text{O}-\text{O}-$  peroxy-functions follows a free-radical chain mechanism initiated by H-atom abstraction from RH by an initiator. The resulting substrate radical rapidly recombines with a molecule  $^3\text{O}_2$  to give  $\text{RO}_2^{\cdot}$ , a peroxy radical. H-atom abstraction from another substrate molecule propagates the chain reaction and delivers the hydroperoxide product ROOH. The formation of cumyl hydroperoxide from cumene follows exactly this mechanism. It is a key step in the industrial Hock process that produces most of the world's phenol (Figure 8, top). The obtained cumyl hydroperoxide is cleaved in a Hock rearrangement to give acetone and phenol.<sup>[39]</sup> The unwanted ageing of ethers to hazardous peroxides by air and sunlight (especially from diisopropyl ether, diethyl ether, THF) also proceeds via such H-atom abstraction mechanisms (Figure 8, middle).<sup>[40]</sup> The resultant hydroperoxides tend to polymerize and pose serious hazard potential; spontaneous detonation regularly causes accidents and injuries.<sup>[40]</sup> In nature, a closely related process (the so-called autoxidation) is an important step of food (e.g., oil) spoilage processes, as unsaturated fatty acids are prone to hydroperoxide formation (Figure 8, bottom). Their subsequent decomposition to short-chain aldehydes, alcohols and acids gives the characteristic odor of rancid food.<sup>[41]</sup> However, synthetic applications of free radical chain reactions with  $^3\text{O}_2$  that operate with good selectivity and high yields are rather rare in chemical laboratories.

The oxidative and radical behavior of  $^3\text{O}_2$  demands that air and oxygen must be excluded when safely handling metallic or organometallic compounds or conducting metal-catalyzed reactions involving reductants ( $\text{H}_2$ , silanes, CO), low-valent



**Figure 8.** Free radical chain reactions of oxygen: cumene process (top), formation of ether hydroperoxides (middle), spoilage of oils (bottom).

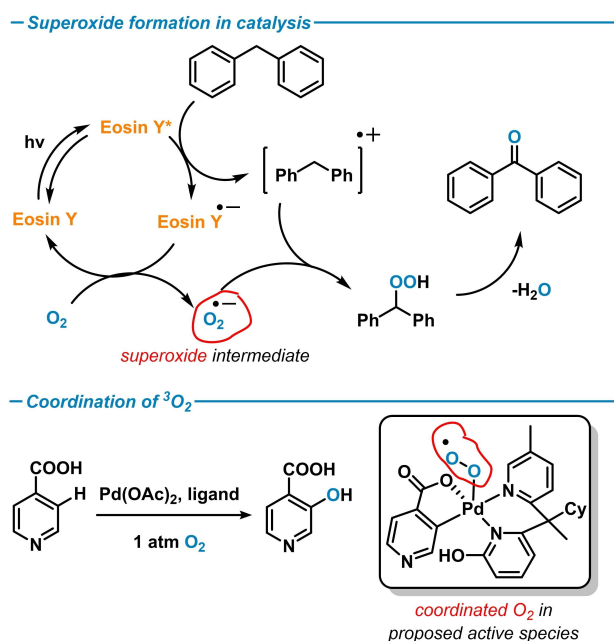
reduced metal complexes [ $\text{Pd/C}$ ,  $\text{Ni}(\text{cod})_2$ , Wilkinson catalyst, etc.], or free radical intermediates (cross-coupling, radical polymerization). An example of a rather selective radical reaction with triplet oxygen is the two-step mechanism with Grignard reagents that operates via single-electron transfer (SET) from the metal to oxygen followed by fast radical-radical coupling. The procedure can be exploited in the synthesis of substituted phenols.<sup>[42]</sup> A range of polyoxometallates, a class of large metal oxide anions, are capable of H-atom abstraction from hydrocarbons; the resulting carbon-centered radicals rapidly react with  $^3\text{O}_2$  to give various oxygenation products.<sup>[43]</sup>

Many modern applications of  $^3\text{O}_2$  in lab-scale synthetic chemistry involve the role as low-molecular-weight, abundant, and inexpensive oxidant and/or oxygen source in transition metal-catalyzed (homocoupling of arenes, oxidative brominations, oxidative annulations, etc.)<sup>[44]</sup> and photocatalyzed reactions that themselves operate via open-shell or radical intermediates.<sup>[45,46]</sup> The individual mechanisms are very diverse but conceptually related to those of the reactions shown above. Many of these recently developed catalytic oxidations mirror biological processes of oxidation and oxygenation but have been tailored to proceed with different catalysts under non-biological reaction conditions to enable wider substrate scopes and specific mechanistic scenarios (e.g., stereocontrol, tolerance of sensitive functional groups, larger scale production). For

example, the eosin Y-catalyzed oxygenation of diphenylmethane to benzophenone is speculated to run via the diphenylmethane radical cation and the superoxide anion (Figure 9, top).<sup>[47]</sup> Superoxide and the radical cation recombine to the hydroperoxide; benzophenone is formed by elimination of water.

With several metal complexes,  $^3\text{O}_2$  shows good coordination ability. The biological respiration mechanisms based on Fe– $\text{O}_2$  heme complexes such as hemoglobin are the most prominent applications from which many synthetic models have been derived from (Figure 3). By choice of the metal, ligands, and reaction conditions, fine tuning of the reactivity of the metal-oxygen complexes can be achieved so that a wide range of selective reactions can be realized. As example of the rapidly developing field of metal-catalyzed C–H bond oxidations, the Pd-catalyzed hydroxylation of isonicotinic acid is shown in Figure 9, bottom. The specifically designed Pd catalyst coordinates  $^3\text{O}_2$  in a linear mode that formally can be viewed as a metallaperoxide species. This electronic state of metal-bonded oxygen selectively oxidizes the C–H bond neighboring the carboxylic acid function, while leaving the pyridine-N and other C–H bonds intact.<sup>[48]</sup>

Recently, the often unselective reactions with triplet oxygen due to over-oxidations have been transferred to new reactor setups, most notably flow reactors. These conditions involve effective mixing of gas phase ( $\text{O}_2$ ) and liquid phase (substrates, catalysts), enable wide variation of reaction parameters ( $\text{O}_2$  pressure, reaction times, temperature), facilitate product separation, and most importantly can be tuned so that over-oxidations are suppressed.<sup>[49]</sup> Simple home-made reactors can be built from inexpensive laboratory equipment (syringes, syringe/HPLC pumps, polymer tubing, valves).<sup>[49b]</sup>



**Figure 9.** Selected reactivities in synthetic chemistry: Formation of superoxide in photoredox catalysis (top), reactivity by coordination (bottom).

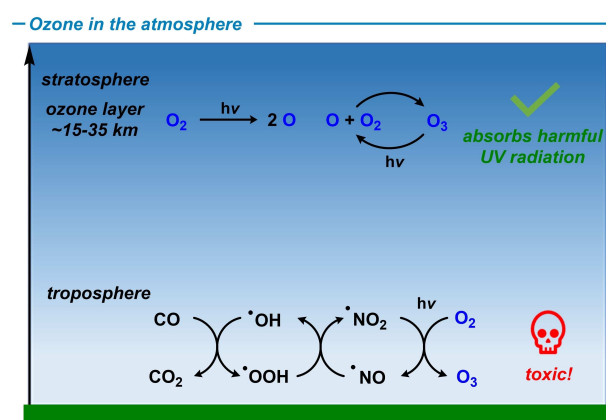
### 3. Ozone ( $\text{O}_3$ )

#### 3.1. General

Ozone, the triatomic allotrope of oxygen, is less stable than triplet oxygen and also much more reactive toward alkenes and alkynes.<sup>[50]</sup> The molecule adopts a bent dipolar structure. At standard conditions,  $\text{O}_3$  is a pale blue gas with a low paramagnetic moment. It has a half-life time between minutes and hours depending on the atmospheric conditions. Its distinctive unpleasant smell has a threshold of about 0.01–0.02 ppm in humans.<sup>[51]</sup> Ozone is a strong oxidant with a standard electrode potential of +2.08 V vs. SHE. Liquid and solid ozone (b.p.:  $-112^\circ\text{C}$ , m.p.:  $-193^\circ\text{C}$ ) are extremely explosive.

#### 3.2. Nature

Ozone mainly occurs in the stratosphere where it forms the so-called “ozone layer” that absorbs most of the ultraviolet part of the sunlight (Figure 10). Both the formation and decomposition of  $\text{O}_3$  are induced by the absorption of UV–B and UV–C light, which also effects irreversible DNA damage in higher organisms when hitting the Earth’s surface. The emission of chlorofluorocarbons led to the anthropogenic ozone layer depletion in the stratosphere. As a result, the amount of solar UV radiation at the Earth’s surface increased. The use of many ozone-depleting substances has been banned by the Montreal protocol.<sup>[52]</sup> On the other hand, the formation of ozone at the Earth surface level, induced by a combination of air pollutants such as nitrogen oxides and hydrocarbons and light, causes serious health threats. The inhalation of  $\text{O}_3$  can lead to vertigo, nosebleed, chest pains, bronchitis, and pulmonary edema.<sup>[53]</sup> The reaction of ozone with organic compounds in the atmosphere such as terpenes can induce the formation of secondary organic aerosols, which are toxic to the human health.<sup>[54]</sup> The presence of highly reactive  $\text{O}_3$  in the troposphere cause damage to many materials such as rubber.<sup>[55]</sup> Therefore, the search for efficient catalysts for the removal of tropospheric ozone is of high interest.<sup>[56]</sup>



**Figure 10.** Ambivalent role of ozone in the atmosphere.

### 3.3. Technology

For commercial use,  $O_3$  is typically generated from diatomic oxygen by exposition to an electrical field or UV light. Low concentrations of ozone can be inadvertently formed via the same processes by household appliances such as air purifiers or printing devices, which is easily perceived by the characteristic smell.<sup>[57]</sup> Due to a maximum half-life of about one day, ozone is typically generated spatially separated from the site of usage in an ozone generator.<sup>[58]</sup> The gas feed of the generator consists of either pure oxygen or pressurized air. Only a small amount of dioxygen is transformed into ozone; typically, an  $O_2/O_3$  stream is fed to the application. The oxidizing properties of ozone are exploited in many application such as chemical oxidations, disinfections, bleaching, or detoxifications (e.g., of cyanide waste) (Figure 11).<sup>[51]</sup> Ozone finds application in environmental remediation; the gas can be injected into the ground to chemically degrade pollutants (aromatics, etc.).<sup>[26]</sup>

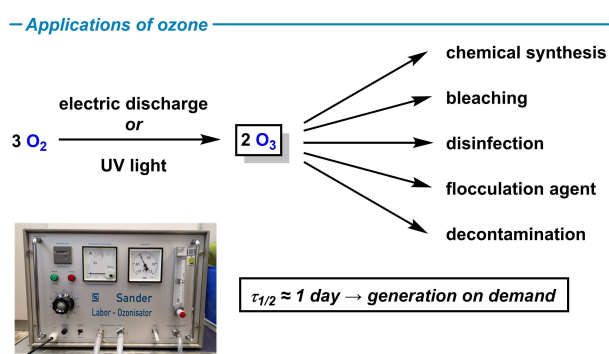


Figure 11. Generation and applications of ozone.

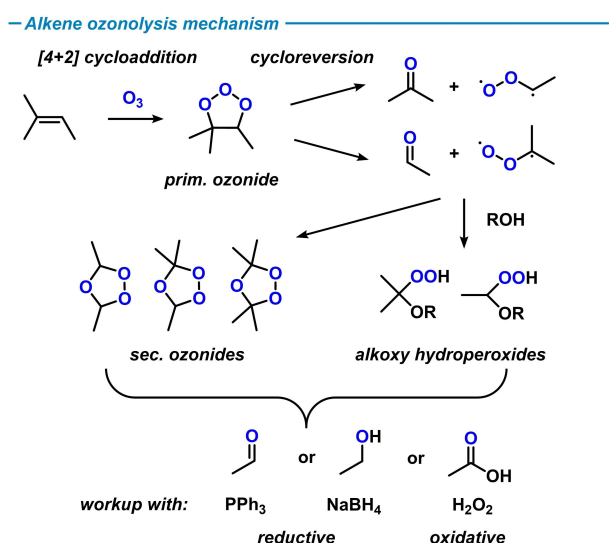


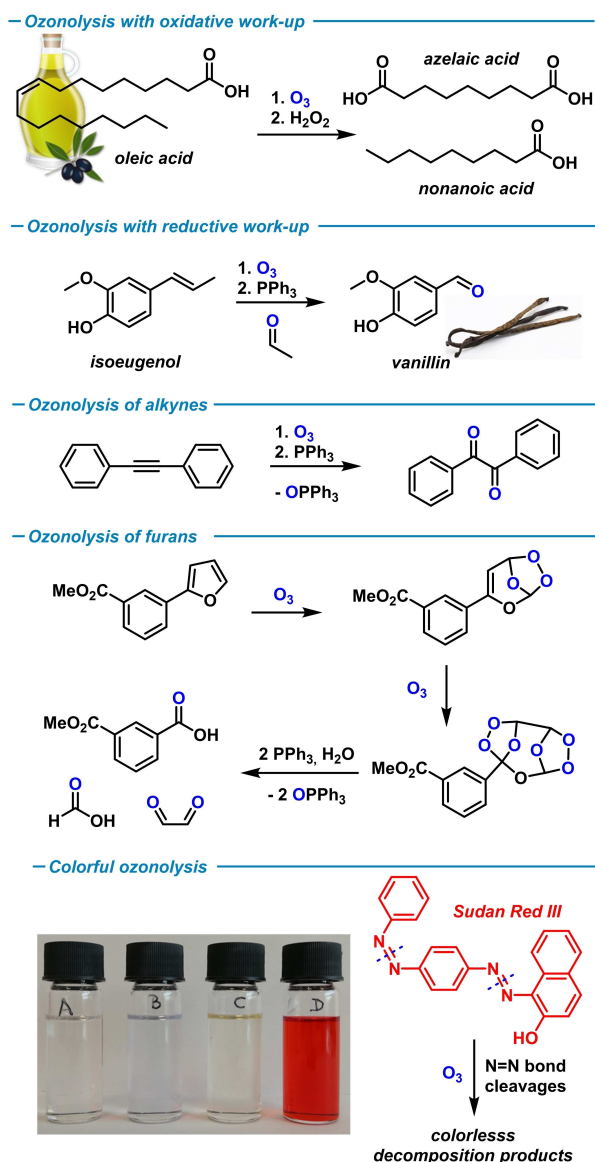
Figure 12. Mechanism of the oxidative C=C cleaving alkene ozonolysis.

### 3.4. Synthesis

Ozone is regularly applied in chemical analyses and chemical syntheses.<sup>[59]</sup> The ozonolysis of alkenes is the major synthesis method involving ozone. Electron-rich C=C double bonds are primarily attacked due to the electrophilicity of ozone. Alkynes and aromatic compounds are less reactive and only oxidized after consumption of all double bonds. The ozonolysis of alkenes is initiated by a [4+2] cycloaddition yielding a primary ozonide heterocycle. Cycloreversion affords a carbonyl and a so-called Criegee intermediate (which can be a biradical or zwitterion). Secondary ozonides are formed by cross-recombination of the two fragments at the other ends (Figure 12). The reaction needs to be terminated with a redox reaction that cleaves the weak O–O bond of the primary oxidation products.<sup>[60]</sup> The work-up procedure determines the products. Aldehydes and alcohols are accessible under reductive conditions, whilst the use of oxidative reagents leads to the formation of carboxylic acids. The presence of short-chain alcohols (methanol, ethanol, etc.) during ozonolysis induces the formation of intermediate hydroperoxyl acetals instead of ozonides. Subsequent work-up, however, delivers the same oxidation products as above.<sup>[61]</sup> Ozonolysis reactions are usually conducted at low temperatures down to  $-78^\circ\text{C}$  to stabilize the labile intermediates. The temperature must not drop below the condensation or freezing point of ozone ( $-112$  and  $-193^\circ\text{C}$ , respectively), since liquid and solid ozone may evaporate explosively. Suitable solvents for ozonolysis reactions include alkanes, halogenated alkanes, ethers, acetone, and short-chain alcohols. The tolerance of oxidation-sensitive functional groups is very low: Amines are converted to nitro compounds and amine-*N*-oxides, phosphines to phosphine oxides, and sulfides to sulfoxides and sulfones. Heteroaromatic compounds (e.g., pyrrole, furan) often decompose in the presence of ozone.<sup>[62,63]</sup>

The ozonolysis of the renewable, bio-based resource oleic acid is run on industrial scale (Figure 13, top). Oxidative work-up is achieved with hydrogen peroxide and provides the two carboxyl acids azelaic acid (ointments, polymers) and nonanoic acid (flavorings, plasticizers, herbicides).<sup>[64,65]</sup> Vanillin is one of the most important food flavor with production scales of more than 20000 tons annually, mostly from chemical synthesis. An early synthetic approach was based on isoeugenol (available from the plant-based eugenol by acid-catalyzed isomerization). Ozonolysis and reductive work-up give vanillin and acetaldehyde (Figure 13).<sup>[66]</sup> Today, more efficient routes have replaced this synthesis. The reaction of ozone with alkynes is far less utilized. Similar intermediates as in the alkene ozonolysis are assumed. Oxidative work-up procedures cleave the intermediates into two carboxylic acids. In case of terminal alkynes, one molecule carbon dioxide is formed.<sup>[67]</sup> Reductive conditions enable the formation of  $\alpha$ -diketones from acetylenes; an example of which is the synthesis of benzil from diphenylacetylene (Figure 13). This synthetically useful reactivity makes  $O_3$  an alternative to more hazardous alkyne oxidizing reagents such as permanganate,  $RuO_2/NaIO_4$ , mercuric salts,  $Ru/t\text{-BuOOH}$ .<sup>[68]</sup> Ozone selectively converts furan derivatives into carboxylates so that furans serve as placeholders for carboxylic acid functions





**Figure 13.** From top to bottom: Ozonolysis of alkenes, alkynes, and furans. Bottom: Visual analysis of reaction courses (A:  $\text{CH}_2\text{Cl}_2$ , B:  $\text{O}_3$  in  $\text{CH}_2\text{Cl}_2$ , C: decomposed Sudan Red III solution, D: Sudan Red III in  $\text{CH}_2\text{Cl}_2$ ).

in many synthesis endeavors (Figure 13). The electron-rich furan is more rapidly attacked by  $\text{O}_3$  than arene rings.<sup>[9]</sup> Further examples of selective ozonolysis of organic molecules have been compiled in the recent literature.<sup>[6,69]</sup>

The progress of ozonolysis reactions can often be tracked visually. Quantitative conversion of the substrate is achieved when the reaction mixture develops a blueish color due to the enrichment with unreacted ozone. Alternatively, brightly colored azo dyes such as Sudan III can be added as indicators (Figure 13, bottom). The diazo groups have a lower reactivity with ozone than  $\text{C}=\text{C}$  double bonds. Upon full consumption of the substrate, the diazo group is oxidized and the dye is fragmented into colorless molecules. Therefore, the discoloration of the red solution indicates the end point of the reaction.<sup>[70,71]</sup>

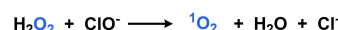
## 4. Singlet Oxygen ( $^1\text{O}_2$ )

### 4.1. General

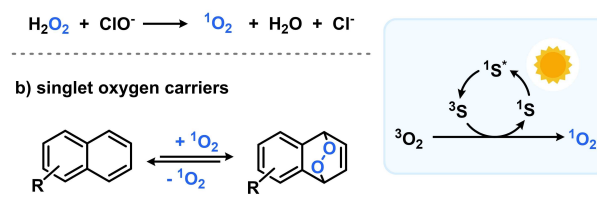
The existence of an “active oxygen species” was first proposed by Kautsky in the 1930 s.<sup>[72a]</sup> General interest in this form of oxygen, the singlet oxygen state  $^1\text{O}_2$ , however started only after the seminal work of Foote and Wexler in 1964.<sup>[72b]</sup> Singlet oxygen is an electrophilic species and reacts preferably with electron-rich  $\text{C}=\text{C}$   $\pi$ -bonds and lone pairs of heteroatoms (N, S, P, Se). In contrast to reactions with the radical reactions of triplet oxygen  $^3\text{O}_2$  and bond cleavage reactions of ozone  $\text{O}_3$ , reactions with  $^1\text{O}_2$  display rather good selectivities under mild reaction conditions. Singlet oxygen has, however, a short lifetime, it returns to its ground state ( $^3\text{O}_2$ ) via radiative deactivation or physical quenching interactions with other molecules. The quenching rate is highly dependent on the stereoelectronic properties of the quencher molecules. Typical lifetimes of  $^1\text{O}_2$  are in the range of milli- to microseconds ( $\tau = 10^{-1}$  s in  $\text{CCl}_4$ ,  $10^{-2}$  s in air,  $10^{-4}$  s in  $\text{CH}_2\text{Cl}_2$ ,  $5 \times 10^{-5}$  s in liquid  $\text{O}_2$ ,  $10^{-5}$  s in MeOH,  $10^{-6}$  s in  $\text{H}_2\text{O}$ ). C–H, N–H, and especially O–H induce rapid electronic-to-vibrational energy transfer. Further quenching modes are charge-transfer deactivation (e.g., by amines) and electronic energy transfer (e.g., by carotenoids).<sup>[72–74]</sup> Due to the short lifetime, effective reactions require the generation of  $^1\text{O}_2$  in situ and proximal to its reaction partner. The direct generation of singlet oxygen from triplet oxygen by light absorption is not very effective due to the low concentration and low extinction coefficient  $\epsilon$  of gaseous oxygen.<sup>[75]</sup> Other methods of generation include the catalyzed decomposition of hydrogen peroxide,<sup>[76]</sup> the deoxygenative release from dioxygen carriers such as anthracenes, and probably the most widely applied technique, the photosensitized production from  $^3\text{O}_2$  catalyzed by an organic dye molecule under visible light irradiation (Figure 14).<sup>[4,77]</sup> Photo-sensitizers

### — Generation of $^1\text{O}_2$ —

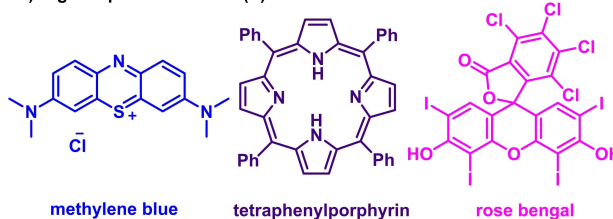
#### a) $\text{H}_2\text{O}_2$ decomposition



#### c) $^1\text{O}_2$ by photosensitization



#### d) organic photosensitizer (S)



**Figure 14.** Generation of singlet oxygen (top) and common organic photosensitizers (bottom).

(e.g., methylene blue, rose bengal, and tetraphenyl-porphyrin) with high extinction coefficients ( $500000 \text{ L mol}^{-1} \text{ cm}^{-1}$ ) and quantum yields (well above 0.5) for  $^1\text{O}_2$  generation are described in literature and readily available.<sup>[78,79]</sup>

#### 4.2. Nature

In nature, the photoexcitation of  $^3\text{O}_2$  to  $^1\text{O}_2$  is a secondary process during the photosynthesis in plant cells with chlorophyll acting as photosensitizer. The high reactivity of  $^1\text{O}_2$  causes oxidative damage to biomolecules such as in the lipid peroxidation or DNA damage and can ultimately lead to programmed cell death (Figure 15, top).<sup>[80]</sup> Singlet oxygen can add to DNA bases such as guanine to form endoperoxides. The

presence of such labile intermediates and their decomposition products lead to erroneous base pairing and mutations (Figure 15, middle).<sup>[81]</sup> Quenching strategies protect the cell structures up to a certain level. Carotenoids act as physical quenchers that deactivate  $^1\text{O}_2$  and dissipate the released energy into heat. Ascorbate, flavonoids, and vitamin B<sub>6</sub> are chemical quenchers that react preferably with  $^1\text{O}_2$  and therefore protect more valuable structures. The quenching mechanism of vitamin B<sub>6</sub> is shown in Figure 15, bottom.<sup>[82]</sup> The presence of  $^1\text{O}_2$  initiates chloroplast-to-nucleus retrograde signaling followed by, among others, increased synthesis of quenching molecules. Thus, it contributes to plant stress responses. The mode of action of certain herbicides is based on an increased  $^1\text{O}_2$  formation that results in cell death and ultimately the death of the plant.<sup>[83–85]</sup>

#### 4.3. Technology

Photodynamic therapies fighting, among others, certain types of cancer mimic the mode of action of oxidative stress in plant cells (Figure 15, top). A medication such as Verteporfin that can act as a photosensitizer is injected intravenously into the patient and disperses throughout the body. Then, the targeted areas are stimulated with a laser inducing the formation of  $^1\text{O}_2$  that effects cell death only in the irradiated areas. Many surgeries and associated treatments can be avoided using photodynamic therapy (Figure 15). In a very similar fashion, photosensitizers can be used to form  $^1\text{O}_2$  for water decontamination.<sup>[86,87]</sup>

$^1\text{O}_2$  also bears a high synthetic value in the synthesis of functional molecules, natural products, and drugs.<sup>[94]</sup> Notable examples are the production of rose oxide and artemisinin (see above). However, applications on industrial scales are very rare, mostly due to low selectivities, short  $^1\text{O}_2$  lifetimes, and poor mixing of such gas-liquid-light reaction settings. Singlet oxygen has a long lifetime in especially harmful and expensive solvents such as  $\text{CDCl}_3$  or  $\text{CCl}_4$ . A promising approach is the use of microreactors that ensure high dispersion of gas, liquid, and light, and short diffusion pathways.<sup>[4,77]</sup>

#### 4.4. Synthesis

Singlet oxygen displays different reaction modes with reactive alkene and heteroatom functions (Figure 16).  $^1\text{O}_2$  engages in [4 + 2] cycloadditions with conjugated *s-cis*-dienes to form endoperoxides, which are often unstable or even explosive. The [2 + 2] cycloaddition with alkenes affords 1,2-dioxetanes that are typically even more unstable and decompose to aldehydes accompanied by UV light irradiation. Isolation of these products is sometimes possible at low temperatures. Furthermore, the singlet oxygen-ene reaction (also called Schenck ene reaction) constitutes a synthetically versatile oxygenation; it was discovered in 1943 by Günther Otto Schenck.<sup>[88,89]</sup> The ene reaction of  $^1\text{O}_2$  with alkenes allows the introduction of hydroperoxyl groups. The reaction proceeds via electrophilic attack of  $^1\text{O}_2$  at the double bond followed by abstraction of an allylic hydrogen.

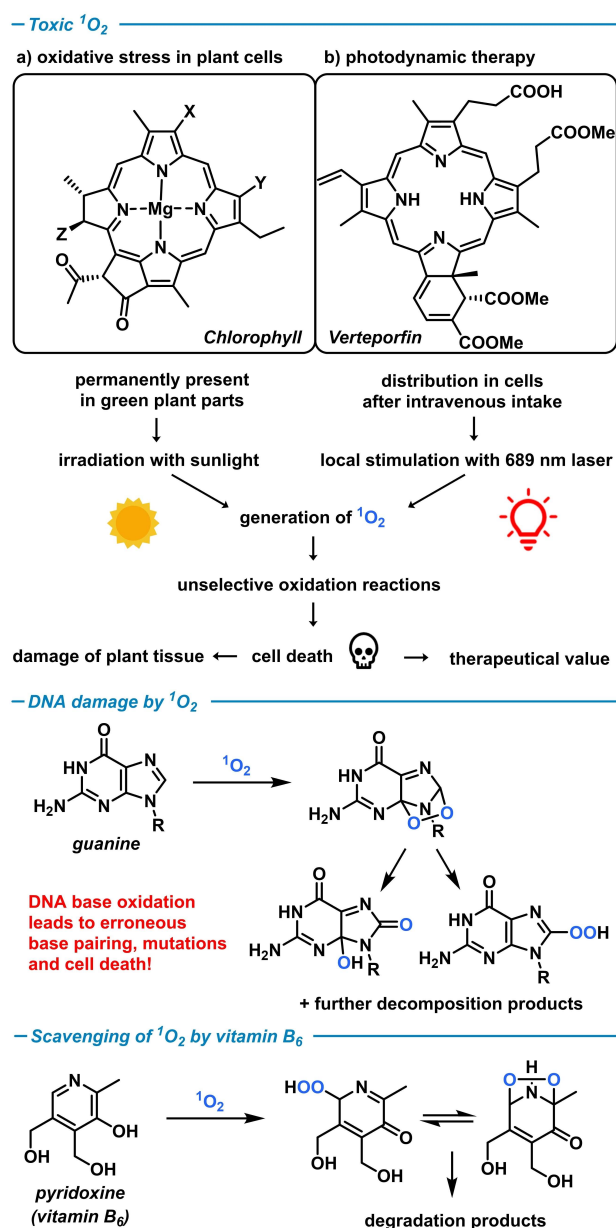


Figure 15. Role of  $^1\text{O}_2$  in oxidative plant stress and photodynamic therapy.

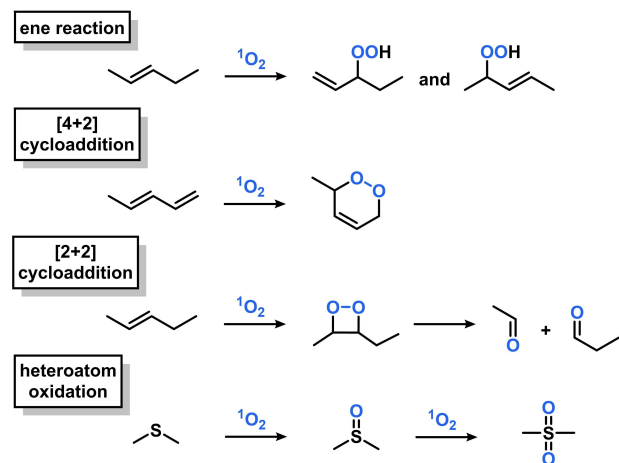
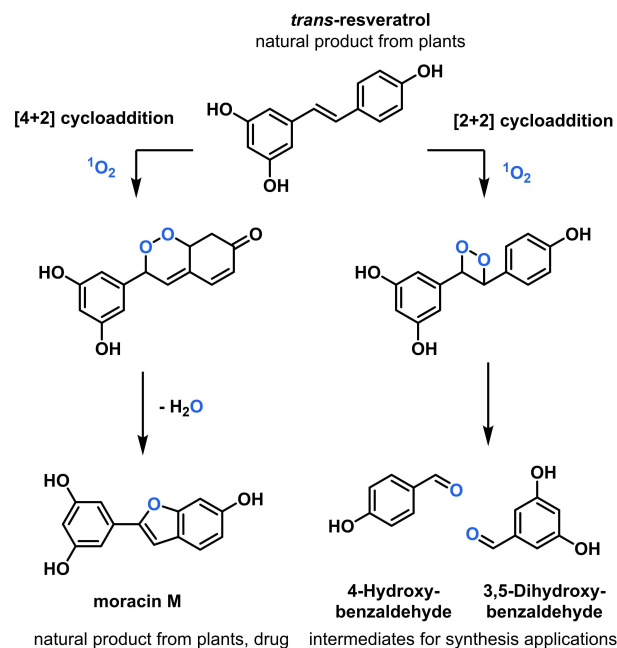
– Reaction types of  $^1\text{O}_2$ 

Figure 16. Reactivities of singlet oxygen with organic molecules.

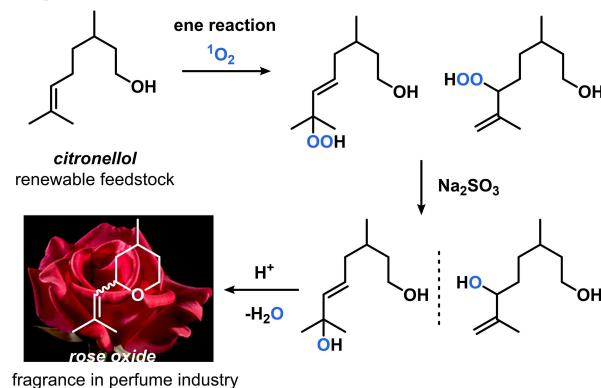
The transition state is described as perepoxide, zwitterion or biradical in nature. The reactivity of an olefin in the ene reaction depends on the electron density and the availability of properly oriented allylic H-atoms in accessible conformations. High levels of regio- and stereocontrol can be achieved under certain conditions, especially in the proximity to directing groups such as amides, alcohols, *tert*-butyl groups, and arenes. Heteroatom-oxidation is a further reaction mode of  $^1\text{O}_2$ . Electron-rich sulfides and phosphines are especially suitable. The oxidation of methylphenylsulfide yields methylphenylsulfoxide and tris(4-methoxyphenyl)phosphine oxide is obtained by the oxidation of tris(4-methoxyphenyl)phosphine.<sup>[90]</sup> The oxidation of metal complexes by  $^1\text{O}_2$  has not been studied in great detail, possibly due to the standard procedures of organometallic and coordination chemistry that typically involve oxygen-free conditions. The formation of oxo complexes has been observed.<sup>[91]</sup> Poorly nucleophilic organometallic reagents may be stable toward  $^1\text{O}_2$ ; an example is the observed ene reaction of allyltin derivatives while the C–Sn bond remained intact.<sup>[92]</sup>

The different reaction modes of  $^1\text{O}_2$  with olefins may directly compete with one another. The ene reaction is usually faster by several orders of magnitude than the [2+2]-cycloaddition to an extent that the dioxetane products are not observable. Compounds that lack allylic hydrogen atoms cannot undergo ene reactions and are therefore preferred substrates for [2+2]-cycloaddition. In a similar fashion, [4+2]-cycloaddition is usually preferred to the [2+2]-reaction in conjugated dienes. An interesting exemption is the reaction of  $^1\text{O}_2$  with *trans*-resveratrol (Figure 17). The incorporation of one double bond into the aromatic system slows down the [4+2]-cycloaddition, about 60% of the substrate is transformed into the endoperoxide. Only 40% material is converted by the [2+2]-cycloaddition; the intermediate dioxetane is highly instable and decomposes into aldehydes.<sup>[93]</sup>

A prominent example of a selective industrial synthesis with singlet oxygen is the annual multi-ton production of rose oxide (Figure 18, top). Singlet oxygen is reacted with  $\beta$ -citronellol to

– Competing  $^1\text{O}_2$  reactionsFigure 17. Competing [4+2]- and [2+2]-cycloaddition of  $^1\text{O}_2$  with *trans*-resveratrol.

## – Synthesis of rose oxide



## – Furfural oxidation

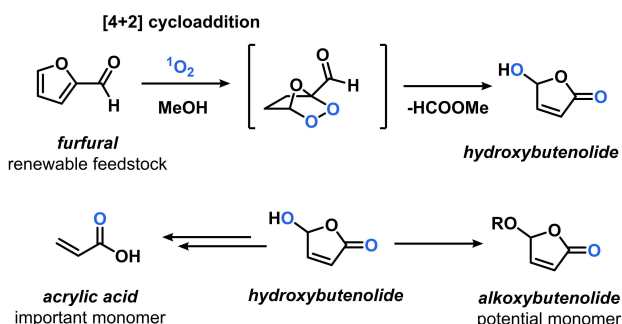


Figure 18. Synthesis of rose oxide from citronellol (top). Furfural oxidation (bottom).

produce allyl hydroperoxides via the Schenck ene allylic oxygenation reaction; two regioisomers are formed in equal

amounts. The reduction of the reaction mixture with sodium sulfite affords two sets of allylic alcohols. Only one of the isomers is used in the subsequent acid-catalyzed rearrangement followed by the elimination of water to give rose oxide as *cis* and *trans* isomers. The product is an important technically produced fragrance.

Research has recently also untapped the potential use of  $^1\text{O}_2$  in the transformation of biomass into feedstock chemicals (Figure 18, bottom). Furfural, that can be easily produced from various glucose-based renewable resources, rapidly reacts with  $^1\text{O}_2$  in methanol solution via [4+2]-cycloaddition to hydroxybutenolide. Etherification with different alcohols affords alkoxybutenolides that were successfully used for coatings. Alternatively, the hydroxy-butenolide can be transformed in few steps into the important monomer building block acrylic acid. This synthesis is an alternative to the industrial petrochemical route to acrylates.<sup>[95,96]</sup>

Singlet oxygen is also used in the synthesis of pharmaceuticals. Ascaridole was the first discovered naturally occurring peroxide and was used as medication against intestinal worms. It can be synthesized by treatment of the natural resource  $\alpha$ -terpinene with  $^1\text{O}_2$  via [4+2]-cycloaddition (Figure 19, top). This process was also the first commercial synthesis employing  $^1\text{O}_2$  and chlorophyll as photosensitizer. Today, the use of ascaridole is limited due to its medical side effects.<sup>[97]</sup> Artemisinin, another endoperoxide-based medication, is an important anti-malaria drug. The direct extraction from *artemisia annua* has a low yield and is very expensive. Therefore, semisynthetic pathways have been developed (Figure 19, bottom). Dihydroartemisinic acid, a more cost-efficient natural precursor, reacts via an  $^1\text{O}_2$ -ene

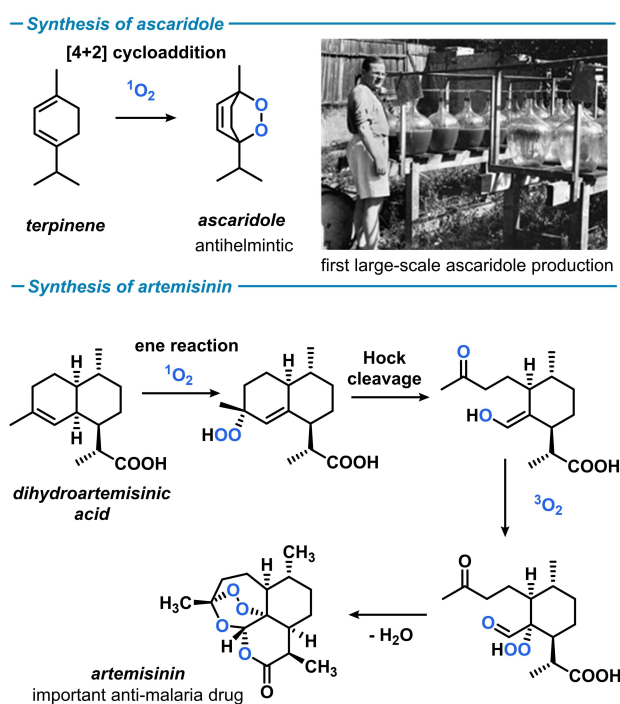
pathway to the allyl hydroperoxide. Hock cleavage, subsequent reaction with  $^3\text{O}_2$ , and water elimination afford artemisinin. This synthesis is a rare example of an oxidation route that includes both oxygen species,  $^1\text{O}_2$  and  $^3\text{O}_2$ .<sup>[98]</sup>

## 5. Key Data of Molecular Oxygen Species for Synthesis Applications

The three oxygen species  $^3\text{O}_2$ ,  $^1\text{O}_2$ , and  $\text{O}_3$  differ in many physical, chemical characteristics, their range of applications, and the operating procedures. The most important information on the reactivity, generation and handling of the oxygen species are compiled in Table 1. The choice of solvent is an important factor in reaction design of the most important mode of reactions where substrates, catalyst, and additives are in solution phase and the gaseous oxygen species is purged into the solution. For reactions with oxygen in general, both the boiling and the flash point of the solvent are important to evaluate the danger of formation of explosive vapor mixtures. A high gas solubility is desirable; oxygen is generally better soluble in nonpolar than in polar solvents. The solubility can be increased by applying gas pressure. The Ostwald coefficient is defined as the ratio of dissolved gas volume [L] per gas-free solvent volume [L] at standard conditions. The melting point of a solvent has to be considered in ozone reactions because they are conducted at low temperatures, and the solvent must not react with ozone. For singlet oxygen reactions, solvents that enable long  $^1\text{O}_2$  lifetimes are favorable. Additionally, environmental and sustainability criteria should be considered. Table 2 gives an overview of the most critical properties of solvents in the context of reactions with oxygen species.

## 6. Summary and Outlook

Molecular oxygen in its different forms plays a pivotal role in many aspects of biology, medicine, technology, and chemistry. Molecular oxygen is the most abundantly available, most inexpensive, and smallest molecule for oxidative transformations on the surface of our planet. The three molecular species  $^3\text{O}_2$ ,  $\text{O}_3$ , and  $^1\text{O}_2$  display distinct physical behavior and chemical reactivities; they can be easily transformed into each other so that a wide variety of applications can be accessed. Numerous transformations of biomass, technical chemicals, pharmaceuticals, household products, foods, and materials rely on oxygen as oxidant (in electronic redox processes) or as oxygen source (for the incorporation of O atoms into molecules). The importance of molecular oxygen in chemistry will most likely increase as its use as an atom-efficient, virtually inexhaustible, inexpensive, and environmentally benign reagent aligns well with the principles of green chemistry and the sustainability development goals of the United Nations. The most important challenges for the use of molecular oxygen species in the realm of modern chemical synthesis revolve around the precise control of their reactivities and reaction mechanisms, the



**Figure 19.** Synthesis of pharmaceuticals: ascaridole (top left) and artemisinin (bottom). G. O. Schenck with ascaridole synthesis “plant”, photograph reprinted from Ref. [99]. Copyright (2003), with permission from Wiley-VCH.

**Table 1.** Compilation of key chemical data of the generation, handling, and reactivities of oxygen species.

Oxygen species	Main reactivities	Temperature range of applications	Supply, generation	Typical reaction additives	Treatment of excess gas	Hazards
triplet oxygen $^3\text{O}_2$	radical coupling; oxidation; CH abstraction	broad	$\text{O}_2$ gas cylinder, compressed air, or ambient air	radical starter or catalyst (transition metal, photo, etc.)	not necessary	oxidizing; formation of explosive atmospheres
ozone $\text{O}_3$	cleavage of multiple bonds (alkene, alkyne, arene); heteroatom oxidation (N, P, S)	$-78-0^\circ\text{C}$	$\text{O}_2$ gas cylinder/compressed air fed to ozone generator on-site	none	reduction of excess ozone, e.g., $\text{Na}_2\text{S}_2\text{O}_3$	toxic; oxidizing; formation of explosive atmospheres
singlet oxygen $^1\text{O}_2$	addition to C=C bonds; ene reaction; heteroatom oxidation (P, S)	RT	$\text{O}_2$ gas cylinder/compressed air with photosensitizer, light source, or chemical generation in situ	none	not necessary	oxidizing; formation of explosive atmospheres

suppression of unwanted over-oxidations or by-product formations, and technological aspects (safety, phase mixing, etc.). The rapid development of ever more effective catalysts, spectroscopic tools, and technological advances such as the implementation of (micro)flow technologies will certainly enable direct oxygenations with the abundantly available and inexpensive molecular oxygen species move to the forefront of modern oxygenation technologies. The consideration of the diverse modes of reactivities and application of molecular oxygen species should take a central role in modern teaching curricula. Future technologies (biomass utilization, waste degradation and recycling, fuel cells, selective chemicals production, medicinal treatments, etc.) will highly depend on oxygen-driven reactions. This Review intended to shed light on the multifaceted applications in an informative and illustrative format for the benefit of students and researchers.

## 7. Exemplary Experiments

Exemplary laboratory experiments with each of the three oxygen species  $^3\text{O}_2$ ,  $\text{O}_3$ , and  $^1\text{O}_2$  are given below that give insight to four aspects of applications: (A) details on the method of generation, (B) reactions that involve characteristic color changes that can be visually observed in classroom demonstrations, (C) experiments that display a general mode of reactivity with “everyday objects”, and (D) experiments illustrating an important application in (modern) chemical synthesis.

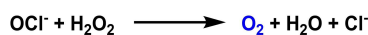
### 7.1. Triplet oxygen ( $^3\text{O}_2$ )

(A) Oxygen generation and proof: Oxygen is liberated by the reaction of many household chemicals, bleach, and hydrogen peroxide solution (Scheme 1); the gas is collected, and its identity is proven by a glowing splint test.<sup>[110]</sup>

(B) The blue bottle experiment: This demonstration experiment shows the oxidation properties of oxygen by inducing several cycles of color change between colorless and blue states of the dye methylene blue (Scheme 2). Variations of the protocol work with green and purple color.<sup>[30,111,112]</sup>

(C) Polymer photodegradation: Household items from polypropylene are exposed to UV-light and atmospheric oxygen (Scheme 3). The gradual degradation of the material properties by oxidation is observed.<sup>[113]</sup>

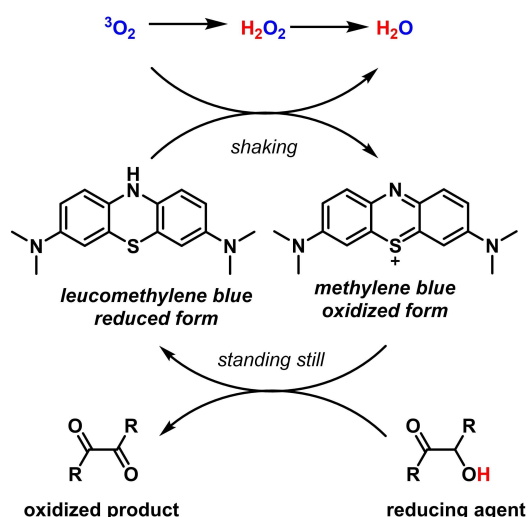
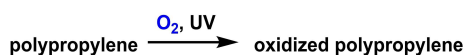
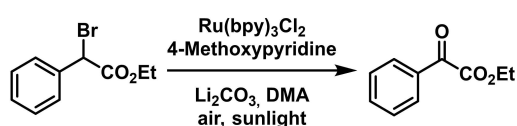
(D) Formation of  $\alpha$ -ketoacids: In this sunlight-catalyzed reaction, oxygen from the air is used as reagent to transform  $\alpha$ -bromoacids into  $\alpha$ -ketoacids (Scheme 4). Only basic laboratory equipment is needed for the reaction.<sup>[114]</sup>

**Scheme 1.** Oxygen generation and proof.

**Table 2.** Selected physical data of common solvents used for reactions with oxygen species.

Solvent	"Greenness" <sup>[a]</sup>	m.p. [°C]	b.p. [°C]	Flash point [°C]	Ostwald coefficient of O <sub>2</sub> <sup>[b]</sup>	<sup>1</sup> O <sub>2</sub> life-time <sup>[b]</sup> [μs]	Reaction with O <sub>3</sub>
acetic acid	problematic	17	118	40	0.18	25	no
acetone	recommended	-95	56	-20	0.28	40	no
acetonitrile	problematic	-45	82	2	0.20	81	no
benzene	highly hazardous	6	80	-11	0.22	32	yes
benzotrile	n.d.	-13	190	75	n.d.	40	yes
<i>tert</i> -butanol	recommended	25	82	11	0.20	34	no <sup>[c]</sup>
chloroform	highly hazardous	-63	61	no	0.28	240	no
1,2-dichloroethane	highly hazardous	-36	84	13	0.18	63	no
dichloromethane	hazardous	-97	40	no	0.26	100	no
diethylether	highly hazardous	-116	35	-45	0.45	34	no
dioxane	hazardous	12	101	12	0.17	25	no
dimethylformamide	hazardous	-61	153	58	0.11	23	no
dimethylsulfoxide	problematic	19	189	89	0.051	6	yes
ethanol	recommended	-114	78	14	0.23	10	no <sup>[c]</sup>
ethyl acetate	recommended	-84	77	-4	0.31	43	no
<i>n</i> -hexane	hazardous	-95	69	-26	0.37	30	no
methanol	recommended	-98	65	12	0.20	10	no <sup>[c]</sup>
isopropanol	recommended	-89	83	12	0.25	n.d.	no <sup>[c]</sup>
tetrahydrofuran	hazardous	-108	66	-14	0.25	20	no
toluene	problematic	-95	111	4	0.22	29	yes
1,2,4-trichlorobenzene	n.d.	17	213	110	n.d.	94	yes
water	recommended	0	100	no	0.030	2	no

[a] Solvent classification based on diverse criteria including availability, physical properties, safety, health, and environmental aspects: recommended > problematic > hazardous > highly hazardous. For a detailed analysis, see Ref. [100]. [b] Rounded average values, limited comparability due to different analytical methods. For Ostwald coefficient of O<sub>2</sub>, see Refs. [101, 102]. For <sup>1</sup>O<sub>2</sub> lifetimes, see Refs. [103–109]. [c] Formation of alkoxy hydroperoxides instead of secondary ozonides possible. n.d. = not determined.

**Scheme 2.** The blue bottle experiment.**Scheme 3.** Polymer photodegradation.**Scheme 4.** Formation of  $\alpha$ -ketoacid.

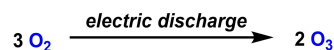
## 7.2. Ozone (O<sub>3</sub>)

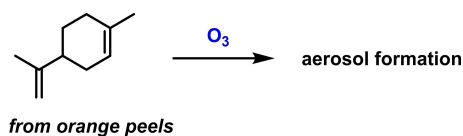
(A) Generation of ozone: A silent discharge ozone generator can be built from common lab items (Scheme 5). Basic technical knowledge is required.<sup>[115]</sup>

(B) Measuring ground-level ozone in the atmosphere: The ozone content of the atmosphere is determined with a home-built mobile set-up. The atmospheric ozone oxidizes an iodide solution (Scheme 6), the concentration of the resulting iodine solution is measured photometrically. Calculations allow the determination of ground-level ozone concentrations.<sup>[116]</sup>

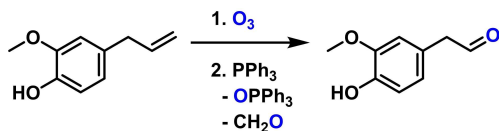
(C) Ozone-induced aerosol formation: In this demonstration experiment, the addition of orange peels into a jar filled with ozone leads to the formation of an aerosol and shows exemplarily the formation of haze in polluted areas (Scheme 7).<sup>[117]</sup>

(D) Ozonolysis of natural products: The ozonolysis of eugenol followed by a reductive work-up serves as an example for the use of ozone in synthetic chemistry (Scheme 8). Basic laboratory UV equipment is required.<sup>[118]</sup>

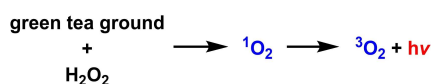
**Scheme 5.** Generation of ozone.**Scheme 6.** Measuring ground-level ozone in the atmosphere.



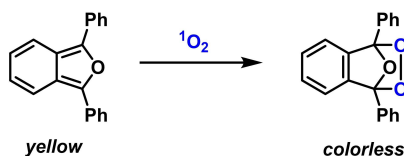
Scheme 7. Ozone-induced aerosol formation.



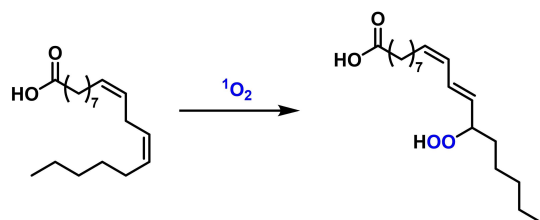
Scheme 8. Ozonolysis of natural products.



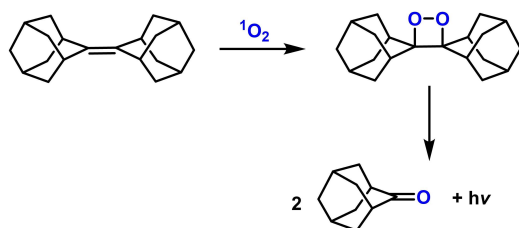
Scheme 9. Generation and phosphorescence of singlet oxygen.



Scheme 10. Cycloaddition-induced color change.



Scheme 11. Peroxidation of lipids.



Scheme 12. Synthesis and chemiluminescence of a stable 1,2-dioxetane.

### 7.3. Singlet oxygen ( $^1\text{O}_2$ )

(A) Generation and phosphorescence of singlet oxygen: The reaction of green tea grounds with aqueous hydrogen peroxide leads to the liberation of  $^1\text{O}_2$ . The return to the triplet ground

state is accompanied by a well-visible red phosphorescence (Scheme 9). No special equipment is needed for this demonstration experiment.<sup>[119]</sup>

(B) Cycloaddition-induced color change: A green solution of diphenyl isbenzofuran (DPBF, yellow) and methylene blue (blue) is treated with in situ generated  $^1\text{O}_2$ . DPBF reacts fast with  $^1\text{O}_2$  to form a colorless product and a color change from green to blue can be observed (Scheme 10).<sup>[120]</sup>

(C) Peroxidation of lipids: The reaction of linoleic acid methyl ester with  $^1\text{O}_2$  to form hydroperoxides is performed and the influence of vitamin E as scavenger is investigated (Scheme 11). Linoleic acid is part of cell walls, and this reactivity illustrates the cell toxicity of  $^1\text{O}_2$ . Basic laboratory equipment and access to an NMR spectrometer are required.<sup>[121]</sup>

(D) Synthesis and chemiluminescence of a stable 1,2-dioxetane: A stable 1,2-dioxetane ring is synthesized and analyzed. The heating of the product leads to the decomposition of the 4-membered ring and a visible chemiluminescence (Scheme 12). This reaction requires laboratory equipment and intermediate/advanced synthetic skills.<sup>[122]</sup>

## Acknowledgements

R.S. is a Kekulé doctoral fellow of the Fonds der Chemischen Industrie (FCI). This work was generously supported by the Deutsche Forschungsgemeinschaft (DFG, JA 1107/9-1). Some pictures, icons, and illustrations were obtained royalty-free from Pixabay. Open Access funding enabled and organized by Projekt DEAL.

## Conflict of Interest

The authors declare no conflict of interest.

## Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

**Keywords:** oxidation · ozone · singlet oxygen · sustainable chemistry · triplet oxygen

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Manuscript received: July 13, 2022

Revised manuscript received: October 8, 2022

Accepted manuscript online: October 10, 2022

Version of record online: November 15, 2022