Asian Journal of Chemistry; Vol. 35, No. 7 (2023), 1539-1562

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2023.27904

REVIEW

Radical Chemistry: A Brief History and Overview

A. MANDAL

Department of Chemistry, Bidhannagar College, Kolkata-700064, India

Corresponding author: E-mail: arabindaju@rediffmail.com

Received: 20 April 2023; *Accepted*: 16 May 2023; *Published online*: 6 July 2023; AJC-21274

The radical chemistry is a fascinating field of research and a review of the applications till date is ready guidance to research groups exploring the area. From the vast field of radical research, the present work mainly is concentrated on biological processes involving metal complexes with bound radicals with the superoxide species as the principal focus. This review on the aspects are distinctly divided into three categories for convenience and ready reference.

Keywords: Radical, Review, Metal bound radical, Superoxide.

INTRODUCTION

Ever since the term 'Radical' was introduced by Lavoisier [1] in 1789, there had been new developments in the science of medicine and physiology. At the University of Michigan in 1900, Moses Gomberg [2] discovered the triphenylmethyl radical, which was the first free radical ever discovered. Atoms, molecules and ions that are capable of independent existence and include one or more unpaired electrons in their outermost atomic or molecular orbitals are known as radicals [3]. This condition is referred to as a singly occupied molecular orbital (SOMO), in molecular orbital theory. Free radicals can be neutral, positively charged or negatively charged. Free radicals are typically indicated in chemical equations by a dot that is positioned directly to the right of the atomic symbol or molecular formula. Due to the unpaired electron present, they are typically reactive(s) [4].

Radicals have established their roles in many of the redox reactions and important synthetic strategies. However, there are few investigations on the appropriate kinetic and mechanistic features of the radical processes. As a result, fundamental questions exist regarding the role of metal ions and radicals in such processes and many important mechanistic issues are yet to be addressed.

As an aerobic organism, our own survival requires the atmosphere of oxygen which is a free radical containing two unpaired electrons. Moreover, an enormous number of other radical species are continuously being generated and destroyed not only inside our body but also the surrounding environment [5]. Atmospheric free radical species are continuously generated due to the effect of harmful radiations from the galaxy, the sun and the earth's radiation belt [6], with large contributions also coming from rising air pollutions, the use of pesticides, and the use of fuel [7].

Radical species are kind of electron reservoirs and in diverse type of chemical reactions like auto-oxidation, polymerization, photochemical reaction and catalysis, they play an imperative role as an intermediate [8]. In many of these redox reactions in radicals bind themselves to the metal ions to facilitate electron transfer processes in the rate determining step [9]. All organic compounds are oxides of compound radicals, but all oxidized things have a single simple radical, as Berzelius noted long ago, a fact that is indicative of the synthetic nature of the universe [10]. The existence and participation of free radical species in different phenomena emphasize that the free radical processes are an integral part of natural biochemical processes and they play a key role in the development of a variety of biological effects [11].

Initially, though the focus on the free radicals was due to their harmful effects behind cellular aging processes, liver damage, carcinogenic and mutagenic changes [12]. Despite these venomous roles, evidences were also found in processes

of DNA replication, respiration and photosynthesis where the radicals are the essential ingredients. They have also been recognized as an essential for the functioning of a number of enzymes like, ribonucleotide reductase [13], lysine-2,3-aminomutase [14], pyruvate-formatelyase [15], prostaglandin H synthase [16], DNA photolyase [17] and dioldehydrase [18]. Galactose oxidase [19], a widely used bioanalytical and histological fungal secretory enzyme represents an interesting example where the enzyme itself is a free radical compound.

The significance of free radicals in the aforementioned areas of biology, ecology and other fundamental parts of daily life is demonstrated by the examples provided. A rapid progress in the field of radical biochemistry was seen during early 1988 [20-23] and over the next three decades, new findings stimulated researcher's interests in the role of dietetic antioxidants in prevention of many fatal diseases like cancer, athrosclerosis, stroke, rheumatoid arthritis and diabetes [24-27].

In living organisms, the formation processes of free radicals and the defense systems to control them are closely related to different metal ions and its complexes [28]. Detailed studies of the enzymatic and non-enzymatic redox reactions involving radical species and metal ions thus demands meticulous attention [29]. Studies of this reaction *in vivo* condition are always difficult because several factors interfere in monitoring them. Thus, one usually takes help of the model or *mimic* complexes to understand the basic mechanisms behind the reactions.

The present review thus discusses the roles of the radical species and the related *mimic* complexes, mainly the metal-bound superoxo complex in different redox, catalytic or enzymatic reactions. The tremendous efforts that have been expended in the area of free radical research in all field of scientific research are thus summarized in three parts: (i) the introduction to different type of radicals and the their reaction mechanism with special emphasize on superoxide anion; (ii) the metal bound radical complexes; and (iii) the chemistry of cobalt(III) bound superoxo radical complex.

Characteristics of radicals: The fundamental difference between a radical species and a molecule lies in the presence of unpaired electrons. However, there are exceptions like dioxygen (O_2) molecule, which has an even number of electrons, which has two unpaired valence electrons in its ground state. The spin multiplicity ($2S + 1$, $S = \Sigma m_s$, where m_s is spin quantum number) of a radical is determined by the number of unpaired electrons each with contribution of ± 1/2 according to their respective parallel or anti parallel spins.

Radical species can be generated by different processes. In simpler cases molecules (with closed shell) in which the inequity between the extents of nuclear attractive force and valence shell electron-electron repulsion force favours the loss of an electron can generate a radical species (open-shell structure). Again, molecules which have both a filled highest occupied molecular orbital (HOMO) containing electrons that repel each other strongly and an energetically favourable lowest unoccupied molecular orbital (LUMO) forms easily an open-shell structure by transferring an electron.

Radicals may also be formed when an electron is removed from the HOMO of a closed-shell parent molecule through oxidation or when one electron is added to the LUMO of the molecule through reduction. The MO that now contains the unpaired electron is defined as the spin occupied molecular orbital (SOMO). The contribution of the SOMO in total bond order is only half of a conventional molecular orbital with two electrons and the presence of the SOMO in radical results in its distinctive chemistry [30].

Types of free radicals

Based on reactivity: According to their reactivities, radicals are classified as (i) stable radical, (ii) persistant radicals and (iii) diradicals.

(i) Stable radicals: Stable free radicals are generally formed from large molecules, commonly organic where the unpaired electron is distributed over a large molecular volume. Examples of this kind are triphenyl radical (TPM) and diphenylpicryl-hydrazl radical (DPPH) [31].

(ii) Persistant radicals: Because of steric crowding around the radical centre, which prevents them from reacting with other molecules, these types of radicals have a lengthy half-life. Examples of these include Gomberg's triphenylmethyl radical, Fremy's salt (potassium nitrosodisulfonate, $[(KSO_3)_2NO^{\bullet}]$, nitroxides ($R_2NO^{\bullet}$) such as TEMPO, TEMPOL, *etc*. [32].

(iii) Diradicals: These are molecules that contain two or more radical centers. The oxygen molecule in the atmosphere has a triplet ground state and is a diradical. Because it is a diradical, atmospheric oxygen has a low reactivity [33].

Based on kinetic activity: Radicals can also be differentiated on the basis of their kinetic activity as (a) transient radicals, (b) persistent radicals and (c) stable radicals.

a. Transient radicals: It undergoes bi-molecular self-reaction at or close to the diffusion-controlled rate limit. Ethyl, isopropyl and *tert*-butyl are transient since for each radical, $E_s = 0$ where, E_s is stabilization energy (as the difference between the strength of the appropriate C-H bond of the parent alkane and the radical in question) [34]. Vinyl and phenyl radicals are also transient their E_s negative.

b. Persistent radicals: It undergoes much slower bi-molecular self-reaction and slow uni-molecular decay reactions (such as β-scissions). Radical can also be described as "persistent" if it has a significantly greater life time in comparison to methyl radical under the same conditions. A radical's lifetime can be significantly shortened by slight "impurities" in the surrounding medium, such as a trace amount of oxygen or a radical scavenger. Radical persistence is dependent on its environment. The rate constant for the bimolecular or unimolecular process by which the radical decays, however, can quantitatively quantify the persistence of a radical under specific experimental conditions. The half-life of the radical provides a measure of its persistence if the decay kinetics are unknown or if the decay involves reaction with a second substance [35].

c. Stable radicals: At room temperature, it doesn't experience decay reactions or if it does, the rates are very small. These "stable" radicals do not react with air and moisture and under ambient conditions they can easily be handled and preserve in the laboratory [36].

Based on structural and electronic properties: According to their structural and electrical characteristics, radicals can be

divided into two classes. The unpaired electron of the vast majority of organic radicals is located in an orbital that is perpendicular to the nearby molecule structure. Such organisms are categorized as radicals. Only a few families of organic radicals have an unpaired electron in an orbital that is located in the plane of the surrounding molecule. Such organisms are categorized as radicals.

Most stable radicals are π-radicals whose examples are N,N-diphenyl-N′-picrylhydrazyl (DPPH), di-*tert*-alkyl nitroxides (*e.g.* TEMPO), 2,2,6,6-tetamethylpiperidin-N-oxy) and pyridinyl [37]. Examples of σ radicals are various iminyls ($R_2C{=}N^{\bullet}$) and iminoxyls ($R_1R_2C{=}NO^{\bullet}$) [38].

Based on radical centre: The simplest free radical is atomic hydrogen with one proton and a single electron. Free radical classified according to have different atoms on which the unpaired electron is centered are: **(I)** oxygen centred radicals, **(II)** sulphur centred radicals, **(III)** carbon centered radical and **(IV)** nitrogen centered radical.

(I) Oxygen centred radicals: These include triplet molecular oxygen ($^3O_2$), singlet oxygen molecule ($^1O_2$), superoxide anion ($O_2^{-\bullet}$), hydroxyl radical ($OH^{\bullet}$).

When oxygen is reduced by one electron to its outer shells, the superoxide free radical anion results. The primary *in vivo* source of superoxide is electron leakage from the mitochondria's electron transport chain [39]. The highly reactive hydroxyl radical reacts with the majority of biomolecules at diffusion-controlled speeds. The hydroxyl radical plays a significant role in radiobiological damage and is many orders of magnitude more reactive than superoxide radicals. Around 1933, Haber & Weiss [40] first proposed that hydroxyl free radicals ($OH^{\bullet}$) were produced when superoxide and hydrogen peroxide react together:

$$O_2^{-\bullet} + H_2O_2 \longrightarrow O_2 + OH^{\bullet} + OH^{-}$$

Singlet oxygen is a reactive oxygen species with considerable oxidizing activity that is not a radical (it does not have an unpaired electron). *In vivo*, it is produced enzymatically by the activity of peroxidases or lipoxigenases [41]. It can also be produced by the application of radiation energy.

(II) Sulphur centred radicals: Sulphur centered radicals like thiyl radical ($R\text{-}S^{\bullet}$) is produced during the oxidation of glutathione [42].

(III) Carbon centered radical: Carbon centered free radical like $^{\bullet}CCl_3$ arises from the interaction of an oxidizing radical with organic molecules [43].

(IV) Nitrogen centered radical: Examples of this kind are nitric oxide ($^{\bullet}NO$), nitrogen dioxide ($^{\bullet}NO_2$) [44].

Source of free radicals: Understanding the sources of free radicals is crucial to comprehending reactivity and its characteristics. Endogenous and external sources are the two main sources of free radicals. Endogenous free radicals are those produced by intracellular processes but operate either inside the cell or are released outside the cell. Irradiation, chemical pollutants and various pharmaceuticals, particularly cancer chemotherapeutic drugs, are examples of exogenous sources of free radicals. Ionizing radiation and other external sources of free radicals are important contributors to the generation of free radicals.

Endogenous source: Endogenous sources of free radicals are mainly of the following types: **(i)** autoxidation, **(ii)** enzymatic oxidation, **(iii)** respiratory burst, **(iv)** subcellular organelles, **(v)** transition metal ions and **(iv)** ischemia reperfusion injury.

(i) Autoxidation: Internal reactions take place in the presence of air, which results in autooxidation. Catechol amines, haemoglobin, myglobin, reduced cytochrome C and thiol are the compounds that go through autoxidation. Any of the above mentoin molecules that have undergone autoxidation cause the reduction of oxygen diradicals and the formation of reactive oxygen species, principally superoxide radicals [45,46].

(ii) Enzymatic oxidation: Enzyme systems such xanthine oxidase (stimulated in ischemia-reperfusion), prostaglandin synthase, lipoxygenase, aldehyde oxidase and amino acid oxidase generate a significant number of free radicals [47].

(iii) Respiratory burst: During phagocytosis, it is a process through which phagocytic cells ingest a significant amount of oxygen. Cytochrome b-245, a membrane-bound flavour protein and a NADPH oxidase system are all present in these phagocytic cells. Enzymes found in cell membranes, such NADPH oxidase, can also exist inactively. Immune complexes and bacteria coated with immunoglobulins cause the enzyme to become active. This activation causes the cell membrane to experience a respiratory burst that produces superoxide [48,49].

(iv) Subcellular organelles: After the natural superoxide dismutase has been removed, it is simple to show that organelles such mitochondria, chloroplasts, microsomes, peroxisomes and nuclei create $O_2^{-\bullet}$. O_2 can receive a single electron to create O^2 due to leaks in the mitochondrial electron transport system [50].

(v) Transition metal ions: Free radical production depends heavily on iron and copper. Transition metal ions participate in the Haber-Weiss reaction that generates $OH^{\bullet}$ from $O_2^{-\bullet}$ and H_2O_2 [51,52].

(vi) Ischemia reperfusion injury: Free radicals are produced as a result of a multitude of consequences that are brought on by ischemia. Hypoxanthine to xanthine and then xanthine to uric acid are normally catalyzed by xanthine oxidase. An electron acceptor is needed as a cofactor in this process. Both the antioxidants superoxide dismutase and glutathione peroxidase are lost during ischemia, in addition to a significant increase in the synthesis of xanthine and xanthine oxidase. $O_2^{-\bullet}$ and H_2O_2 are generated as a result of the molecular oxygen given during reperfusion acting as an electron acceptor [53].

Exogenous source: Exogenous sources of free radicals are mainly of the following types: **(i)** drugs, **(ii)** radiation, **(iii)** tobacco smoking, **(iv)** inorganic particles and **(v)** gases.

(i) Drugs: In the presence of oxygen, a number of medicines can boost the generation of free radicals. These medications include methotrexate, which has pro-oxidant action, antineoplastic medicines like bleomycin, anthracyclines (adriamycin) and antibiotics that depend on quinol groups, bound metals, or nitrofurantion for activity [54,55].

(ii) Radiation: When cellular components like water are exposed to electromagnetic radiation, such as X-rays and γ-rays as well as particulate radiation, such as electrons, photons, neutrons, α and β-particles, primary radicals are produced [56].

(iii) Tobacco smoking: Tobacco smoke contains oxidants that, through a process connected to oxidative stress, significantly deplete intracellular antioxidants in the lung cells. Algehudes epoxides, peroxide and other free radicals with long enough half-lives are among these oxidants that can harm alveoli. Additionally, the smoke contains nitric oxide, peroxyl radicals and carbon-centered radicals [57].

(iv) Inorganic particles: Mineral dust, which includes inorganic particles such as asbestos, quartz and silica, can cause lung damage that is at least partially thought to be mediated by free radicals. Through microhemorrhages, asbestos fibres frequently release iron from haemoglobin, which can promote the production of hydroxyl radicals [58].

(v) Gases: Although ozone itself is not a free radical, it can react with biological substrates to produce free radicals [59].

Roles of free radicals in atmosphere: Free radicals are now generally acknowledged to play a significant influence in both the chemistry of naturally occurring and contaminated atmospheres. Carbonyl molecules, primarily aldehydes and ketones, which are released into the atmosphere as primary pollutants (from burning vegetation, for example) or as reaction intermediates from the photo-oxidation of volatile organic compounds (VOC) by NOx, are significant precursors of radicals. An important resource of free radicals in the environment is the photolysis of organic molecules that are partially oxygenated [60]. In most cases, the photolysis of ozone at wavelengths below 3335 nm results in an excited oxygen atom, which then produces hydroxyl radicals in the atmosphere [61]. This departed O (^{1}D) atom either becomes a ground-state oxygen O (^{3}P) atom through quenching or has a reaction with water vapour to form OH$^\bullet$. The photolysis of nitrous acid (HONO), formaldehyde and other carbonyls in the presence of NO are two additional sources of OH$^\bullet$ in the troposphere. The intermediate alkyl radicals quickly react with ambient oxygen to generate alkyl peroxy radicals during the breakdown of VOC (RO_2, HO_2 or RH-OH-O_2). Alkoxy radicals are created when peroxy radicals interact with NO, NO_3 or other peroxy radicals (RO, OH or RH-OH-O). Many alkoxy radicals revert to peroxy radicals, however they do so with a decreased alkyl group. Uptill HOx radicals are accessible, this cycle will continue [62].

Reactive oxygen/nitrogen species and its role in biological system

Reactive oxygen species (ROS): The first free radicals to be identified in living materials are ROS. It is a general word that encompasses both non-radical derivatives of oxygen, such as hydrogen peroxide (H_2O_2), singlet oxygen and hypochlorous acid, as well as oxygen-centered radicals like $O_2^{-\bullet}$ and $^\bullet$OH (HOCl).

(a) Singlet oxygen and ozone: By interacting with triplet-excited molecules, such as excited protoporphyrin IX, ground state oxygen can also be transformed into singlet oxygen ($^1O_2$). Singlet oxygen is a non-radical species with outer electrons in antiparallel spins that has a relatively long life (microseconds). Due to the lack of spin constraint, $^1O_2$ has a high oxidizing power and can damage DNA, carotenoids, amino acid residues in proteins and membrane polyunsaturated fatty acids (PUFAs) [63]. Another non-radical triatomic species is ozone. Ozone is a potent oxidizing agent due to its E^0 value, which allows it to interact with tiny antioxidants like vitamin C and uric acid as well as proteins, DNA, PUFAs and other molecules [64].

(b) Superoxide and hydrogen peroxide: A notable illustration of a free radical species that can function as an oxidizing or reducing agent is superoxide, $O_2^{-\bullet}$, which can convert nicotinamide adenine dinucleotide (NADH) from its reduced form to its oxidized form, NAD (NAD^+). $O_2^{-\bullet}$ can diminish iron-sulfur cluster-containing enzymes, cytochrome C, ferritin and Fe^{3+} bound to citrate (such as aconitase). The protonated form of $O_2^{-\bullet}$, the hydroperoxyl radical (HOO$^\bullet$), which may remove hydrogen from PUFAs, has a lower reduction potential than $O_2^{-\bullet}$. A rather ineffective oxidizing agent, hydrogen peroxide has an E^0 value of (+0.32 V for the pair H_2O_2/$^\bullet$OH) [65].

(c) Hydroxyl radical: It is now understood that a large portion of H_2O_2's oxidizing effects on DNA, lipids and proteins were generated by its interaction with transition metals, primarily Fe^{2+} and Cu^{2+}, which produced the hydroxyl radical, $^\bullet$OH or other highly reactive oxo-metallic species like ferryl (Fe^{4+}=O). The O-O bond in H_2O_2 is broken by a single electron reduction, releasing $^\bullet$OH and OH^-. Additionally, radiation-induced homolysis of water or H_2O_2 as well as the interaction of hypochlorous acid with $O_2^{-\bullet}$ can produce $^\bullet$OH [66].

$$H_2O_2 + Fe^{2+} \text{ (or } Cu^+) \longrightarrow Fe^{3+} \text{ (or } Cu^{2+}) + OH^- + {}^\bullet OH$$

$$H_2O_2 + \text{energy} \longrightarrow 2\,{}^\bullet OH$$

$$HOCl + O_2^{-\bullet} \longrightarrow Cl^- + O_2 + {}^\bullet OH$$

Hydroxyl radicals play a role in the oxidation and destruction of proteins, nuclear DNA and mitrochondrial DNA in addition to the beginning of lipid peroxidation of biological membranes. Relevant targets of OH include ribonucleic acid (RNA) and carbohydrates [67].

Reactive nitrogen species (RNO)

a. Nitric oxide: A highly reactive radical species, nitrogen dioxide ($^\bullet NO_2$), is produced when nitric oxide ($^\bullet$NO), which has an unpaired electron, interacts with oxygen very slowly. The primary break-down product of NO is nitrite (NO_2), which is formed as a result of further interactions between NO_2 and NO. Under specific circumstances, NO is quite stable *in vitro*, yet it vanishes *in vivo* in a matter of seconds. Nitric oxide produces peroxynitrite [O=NOO, typically written as ONOO-] upon contact with $O_2^{-\bullet}$ when it reacts fast with the heme group of haemoglobin.

b. Peroxynitrite: poisonous peroxynitrite is an anion which is highly stable and does not have radical properties. The majority of biological molecules, including DNA, RNA, proteins and lipids, can be oxidized by it [68].

c. Nitrosothiols (or thionitrates): S-nitrosoglutathione, a molecule having signalling capabilities, is produced when the radical form of glutathione (thiyl radical, RS$^\bullet$) reacts with NO [69].

In living things, free radicals and other ROS and RNS have some physiological and pathological impacts. Redox-responsive

signalling pathways regulate numerous physiological processes. The regulation of NO production, ROS creation by phagocytic NAD(P)H oxidase (oxidative burst) and ROS production by NAD(P)H oxidases in non-phagocytic cells are a few examples [70].

Antioxidants: defense against oxidants or free radicals: Free radicals are produced when radicals interact with oxygen and function in the cells at low but detectable concentrations. The equilibrium between the rates of synthesis and elimination of free radicals by various antioxidants determines the amounts of these molecules in a "steady state." Therefore, a cell's redox status and oscillation dictate how well it functions. Ironically, certain ROS-mediated processes actually shield cells from ROS-caused harm and restore or preserve "redox balance," also known as redox homeostasis [71]. However, because the ROS in higher concentrations are what cause cellular damage, humans have developed an incredibly complex and powerful antioxidant defence system to shield the body's cells and organ systems from free radical damage. Antioxidants are substances that, despite frequently being oxidized themselves, at low concentrations considerably limit or delay the oxidative process. By preserving radox equilibrium, endogenous and exogenous antioxidants are used to combat free radicals and defend the organism from them [72]. These antioxidants can be divided into various categories. In Table-1, antioxidants are classified in depth, while Table-2 lists the functions of several antioxidants and their sources.

All aerobic living forms are equipped with a very complex defensive system to control the damage of cell constituents by harmful ROS and RNS. The importance of antioxidant defense system can be emphasized by the fact that some of enzymatic defense systems have ancient origin and they have the conserved amino acid sequences across wide phylogenetic range of bacteria to human. The antioxidant defense systems of living forms can be divided into four subclasses [73]:

a. Primary antioxidant defense systems of enzymatic or non-enzymatic nature that directly deal with ROS.

b. Auxilliary defenses systems that support the function of the primary antioxidant systems (*e.g.* by recycling or synthesizing substrates of antioxidant enzymes).

c. Metal-complexing proteins/enzymes (*e.g.* ferritin, transferring, ceruloplasmin and low molecular weight compounds) that prevent or minimize the participation of iron or copper (and other heavy metals) in free radical generation.

d. Enzymatic repairing systems that repair biomolecules damaged by ROS and RNS.

Animals do not produce the majority of their endogenous enzymatic antioxidant defence mechanisms; instead, these defences are obtained from their diet. Although only a small number of them exhibit pro-oxidant activity *in vitro*, the plant and bacterial worlds contain an enormous variety of diverse chemicals with potential antioxidant activity (mostly phenolic and carotenoid groups). The antioxidant defence system is thought to include several metals as well as some non-metal components (like selenium). They are necessary cofactors for a number of antioxidant enzymes that maintain the life of the organisms. For instance, ceruloplasmin and superoxidemustase (CuZnSOD) in the human body require copper and zinc [74]. Large reserves of endogenous antioxidants such glutathione, vitamin C and E are present in body neutrophils. Because the stored antioxidants are present during phagocytosis in a reduced form, neutrophil oxidative suicide is avoided. A tripeptide called glutathione (glutamyl-cysteinyl-glycine) targets radical species with a highly reactive free sulphydryl group (SH). A redox cycle involving glutathione reductase and the electron acceptor NADPH regenerates the reduced form of glutathione after it

TABLE-1
CATEGORIES OF ANTIOXIDANTS

(A) CLASSIFICATION BASED UPON THEIR NATURE	1. Enzymatic antioxidant	Glutathione peroxidase (GPx), Catalase (CAT), Superoxide dismutase (SOD) and Glutathione reductase (GR).
	2. Non-enzymatic antioxidant	(a) Metabolic antioxidant. Reduced Glutathione (GSH), L-arginine, Lipoid acid, Coenzyme Q_{10}, Uric acid, melatonin, bilirubin, metal-chelating proteins, transferrin, *etc.*
		(b) Nutrient antioxidant. Vitamine-E, vitamine-C, carotenoids, trace metals (selenium, manganese, zinc), flavonoids, omega-3 and omega-6 fatty acids, *etc*.
(B) CATEGORIES BASED UPON SOURCE	1. Endogeneous antioxidant	Bilirubin, Glutathione, lipoic acids, N-acetyl), uric acid, cysteine, NADPH and NADH, ubiquinone (Coenzyme Q_{10}, enzyme (SOD, CAT, GPx, GR).
	2. Dietary	Vitamin C, Vitamin E, β-carotene and other carotenoids and oxycarotenoids (lycopene and lutein), polyphenols (flavonoids, flavones, flavonols and proanthocyanidins)
	3. Metal binding proteins	Copper is present in albumin, ceruloplasmin, metallothionein, ferritin, myoglobin and transferrin. Iron is also present.
(C) CLASSIFICATION BASED MECHANISM OF ACTION	1. Catalytic system to neutralise or divert ROS	SOD, CAT, GPx.
	2. Metal ion binding and inactivation stop the Haber-Weiss reaction from producing ROS.	Carculoplasmin, catechins and ferritin.
	3. Antioxidants that are self-suicidal and break chains scavenge and eliminate ROS.	Flavonoids, vitamin E, uric acid, vitamin C and glutathione.
	4. Quenching ROS, chemical traps/sinks to 'absorb' energy	Carotenoids, anthocyanidins.

TABLE-2
DIFFERENT ANTIOXIDANTS AND THEIR EFFECTS

Antioxidants	Location/Sources	Remarks
Superoxide dismutase (SOD)	Cytosol, mitocondria, nucleus, plasma	Superoxide dismutation to hydrogen peroxide (H_2O_2)
Catalase (CAT)	Peroxisomes	H_2O_2 dismutation to produce water and molecule oxygen
Glutathione peroxidase (GPx)	Cytosol, mitochondria	Reduction of H_2O_2 and other hydroperoxides, lipid peroxides, lipoxygenase products
Glutathione reductase (GR)	Cytosol, mitochondria	Low molecular weight disulfides are reduced
Glutathione (GSH)	Most eukyrotic cells contain a tripeptide in high amounts. It is a component of cells' cytoplasm and the main intracellular nonproteinthiol molecule.	In the GSH redox cycle, the substrate functions as a reductant, reducing H_2O_2 instantly to water along with the production of GSSG. Additionally, it directly engages in a radical transfer reaction with superoxide anion, hydroxyl and alkoxyl radicals to prevent tissue damage. GSH has the ability to directly or nzymatically scavenge ROS *via* GPx.
Uric acid	Wide distribution	A potent antioxidant, uric acid binds transition metals and scavenges singlet oxygen as well as radicals such the superoxide anion, hydroxyl and alkoxyl radicals.
Cysteine	Wide distribution	Additionally essential for the creation of glutathione, cysteine can also decrease organic molecules by accepting e- from SH groups. N-acetyl-L-cysteine (NAC), a derivative of cysteine, is utilized in medicine as a precursor to glutathione and a scavenger of H_2O_2 and peroxide.
Vitamin E	Present in cells and mitochondrial membranes in relatively high amounts. found in amla (Indian gooseberry), lemon, oranges, cashew nuts, germinated pulses, rasins, olive oil, palm oil and groundnut oil.	Superoxide is directly neutralized, hydroxyl radicals are upregulated, antioxidant enzymes are increased and the chain process of lipid peroxidation is broken.
Vitamin C	ICF and ECF are additionally present in lemons, oranges, olive and palm oils, cashew nuts and germination-stage pulses.	Superoxide, hydroxyl radicals, oxidants produced by activated neutrophils and vitamin E regeneration

reacts with the radicals [75]. The main lipid-soluble antioxidant, vitamin E (α-tocopherol), is essential for shielding membranes from oxidative damage. By lowering radicals, vitamin C (ascorbic acid) also functions as an antioxidant [76].

Oxidative stress: The generation of reactive species and antioxidant molecules almost balance each other out in a healthy human organism [77]. It has been discovered that even in healthy tissues, little amounts of free radicals damage biomolecules. In reality, the reactive species attack cannot be totally thwarted by the antioxidant defence system; hence, a mending system is also required to reduce the amounts of damage. Oxidative stress is a condition when there is an imbalance between the generation of reactive species and the antioxidant defence system. Oxidative stress can be caused by a variety of factors:

(a). Mutations that reduce the production of enzyme antioxidants such CuZnSOD, MmSOD and GSHPX. Oxidative stress can also result from dietary antioxidant and other key nutrient deficiencies.

(b). Exposure to highly reactive species known as toxins, such as NO_2 gas, which cause the activation of "natural" ROS/RNS-producing mechanisms.

Biomolecules subsequently subjected to oxidative damage may be significantly affected, contributing to tissue damage and the pathophysiology of a number of human diseases. For instance, tumultuous blood flow, viral infections, or circulating chemicals might harm the arterial endothelium and start the atherosclerosis process.

Superoxide radical: Because of the anion $O^{2-\bullet}$ extraordinary degree of reactivity, particularly as a potent oxidant and a catalyst for radical processes, the term "superoxide" was coined. The radical anion $O^{2-\bullet}$'s potassium salt was given the name "superoxide" for the first time in 1934 [78], despite the fact that the phrase has nothing to do with the anion's chemical reactivity. It was selected to highlight the stoichiometric distinction between KO_2 and other metal-oxo compounds, such as sodium hydroxide (NaOH), oxygen (Na_2O), peroxide (Na_2O_2), hydroperoxide (NaO_2H) and oxide (NaO_3) (ozonide). Superoxide generated a little bit more interest than other substances for a long time [79]. The invention of self-contained breathing gear that utilized KO_2 sparked earlier interest in superoxide chemistry [80]. KO_2 (suspended in non-polar solvents) was found to be rather unreactive and of limited use in organic synthesis by a number of organizations in the early 1960s [81-83]. A few researchers noted that superoxide in aqueous solution is a comparatively harmless species throughout the same time period [84,85]. However, two publications that requisitioned the superoxide reactivity were published in 1969. The first one [86] discussed the ESR research of superoxide during an enzymatic process involving dioxygen and the second [87] discussed the catalytic activity of metalloproteins such superoxide dismutases (SOD) in the disproportionation of superoxide ion. Thus, it was determined that the biological role of SOD was to defend live cells against the harmful effects of superoxide species [87].

$$2O_2^- + 2H^+ \xrightarrow{SOD} O_2 + H_2O_2$$

Studies of superoxide reactivity in relation to the field of metabolic processes have received new impetus in the last 20 years as a result of the development of various preparative methods and advancements in analytical techniques that have

revealed the possibility that superoxide might be an important intermediate species. Superoxide has been reported to be produced *in vivo* as an intermediate or byproduct in some auto-oxidation events, however bi- metallo-proteins (superoxide dismutase) that catalyze its disproportionation into H_2O_2 and O_2 usually shorten superoxide's lifespan in bio systems [88,89]. Such proteins are believed to have evolved to shield organisms from superoxide toxicity, though the specifics of how they do this are still up for debate [88,90]. The continuation of experimental investigations on the reactions of this anion and its derivatives is largely due to the intervention of superoxide, $O_2^{\bullet-}$ in biological processes [91]. Superoxide has been connected to several auto-oxidations as an intermediary [92] as well as being a metabolic byproduct from aerobic organisms [93]. Rapid-freezing ESR technology has recently offered strong proof that a significant amount of $O_2^{\bullet-}$ species are produced by the univalent reduction of molecule oxygen in biological systems [94]. $O_2^{\bullet-}$ is a byproduct of several flavoproteins, enzymes like xanthine oxidase, reduced flavins and other enzymes that can sustain the flow of electrons from enzymes to electron acceptors like cythochrome C or participate in chemical reactions facilitated by oxygenases [95].

Physical properties: The equilibrium between HO_2 and its conjugate base in aqueous solution, $O_2^{\bullet-}$ has a pK_a value of ~ 4.8 [96,97]:

$$HO_2^{\bullet} \rightleftharpoons O_2^{-} + H^{+}; \quad K_1 = 1.6 \times 10^{-5}\ M$$

Both HO_2 and $O_2^{\bullet-}$ oxy-radicals absorb light in the ultraviolet region with a maxima at 225 and 245 nm with molar extinction coefficient (ε) values of 1400 and 2350 $M^{-1}\ cm^{-1}$, respectively. In aqueous solution, the reduction potential, E^0 (*vs.* NHE) for O_2, O_2^- and HO_2 with unit concentration used as the standard state for all reactants and products are as follows:

$$O_2 + e^- \rightarrow O_2^-;\ E^0 = -0.16\ V \text{ at pH } 7.0$$

$$O_2 + H^+ + e^- \rightarrow HO_2;\ E^0 = +0.12\ V \text{ at pH } 0.0$$

$$O_2^- + 2H^+ + e^- \rightarrow H_2O_2;\ E^0 = +0.89\ V \text{ at pH } 7.0$$

$$HO_2 + H^+ + e^- \rightarrow H_2O_2;\ E^0 = +1.44\ V \text{ at pH } 0.0$$

If the unit pressure for the standard state of dioxygen (O_2), is utilized, the first two E_0 values are moved by - 0.17 V [98,99].

In a solid state the O-O bond length of $O_2^{\bullet-}$ is 1.33 Å which corresponds to a bond order of 1.5 [100]. The IR stretching frequency for $O_2^{\bullet-}$ is 1145 cm^{-1} in contrast to 1556 cm^{-1} for O_2 and 770 cm^{-1} for O_2^{2-} [101,102].

In acetonitrile with 0.1 M tetrapropylammonium perchlorate, $O_2^{\bullet-}$ shows a single absorption peak (λ_{max} = 255 nm, ε = 1460 $M^{-1}\ cm^{-1}$) and in frozen glasses of this same solution at 77 K, O_2^- produces ESR signals with $g_\perp = 2.008$ and $g_\parallel = 2.083$ [103].

When paired with the value for the O_2/H_2O_2 couple at pH 7 (E^0 = +0.27 V) [104] in aqueous media (0.1M sodium formate, 2 mM phosphate buffer), an approximation of the value for the $O_2^{\bullet-}/H_2O_2$ couple at pH 7 can be determined [105].

$$O_2^{\bullet-} + 2H^+ + e^- \rightarrow H_2O_2;\ E^0 = +0.87\ V$$

Chemical properties: The disproportion of $O_2^{\bullet-}$ and perhydroxyl radical yields hydrogen peroxide and dioxygen *via* a pH dependent mechanism shown below:

Acid base equlibrium:

$$HO_2^{\bullet} \longrightarrow O_2^{\bullet-} + H^+ \qquad pK_a = 4.8$$

Natural disproportionation:

$$HO_2^{\bullet} + HO_2^{\bullet} \longrightarrow H_2O_2 + O_2 \qquad k = 8.6 \times 10^5\ M^{-1}\ s^{-1}$$

$$HO_2^{\bullet} + O_2^{\bullet-} + H^+ \longrightarrow H_2O_2 + O_2 \qquad k = 1.0 \times 10^8\ M^{-1}\ s^{-1}$$

$$O_2^{\bullet-} + O_2^{\bullet-} + 2H^+ \longrightarrow H_2O_2 + O_2 \qquad k < 0.3\ M^{-1}\ s^{-1}$$

$O_2^{-\bullet}$ anion can rapidly oxidize substrates like hydroquinones through proton-coupled electron transfer mechanism resulting in formation of hydroperoxide anion, HO_2^- [106]. As an alternative, $O_2^{-\bullet}$ can oxidize a metal ion by producing a metal peroxo complex in an oxidative addition reaction (the metal-bound peroxide is more stable than the protonated one), which upon dissociation causes the metal ion to become completely oxidized [107].

Superoxide ion also displays the following properties

a. Nucleophilicity: Superoxide ion has a strong solvation followed by a quick hydrolysis and disproportionation, which makes it a potent nucleophile in aprotic solvents but not in water. The first report of $O_2^{\bullet-}$'s nucleophilic reactivity toward alkyl halides was made in 1970 [108]. These and further kinetic investigations [109] verified that the reaction is first order in substrate concentration and that, for alkyl halides and tosylates, the rate increases as primary > secondary >> tertiary. Primary and secondary alkyl halides react in aprotic solvents *via* a multi-step SN_2 process to primarily produce dialkyl peroxides along with other elimination products [110]. When $O^{2-\bullet}$ attacks the carbonyl carbon of esters or acyl halides to produce carboxylic acid anions, alcohols or diacyl peroxides, it also functions as a nucleophile. The carbonyl carbon undergoes nucleophilic addition when -keto, -hydroxy and -halo carbonyl compounds react with $O^{2-\bullet}$. By oxidative cleavage, carboxylic acid is produced from the location.

b. One-electron reductant: One-electron reducing agent is $O^{2-\bullet}$'s most recognisable reaction. For instance, 3,5-di-*tert*-butylquinone (DTBQ) and $O^{2-\bullet}$ react in the presence of DMF to produce the semiquinone anion radical DTBSQ- as the main byproduct [111]. For complexes of transition metal ions like Cu(II), Mn(III) and Fe(III), $O^{2-\bullet}$ also works well as a reducer. Recent studies have shown that the electron-donating property of $O^{2-\bullet}$ allows it to decrease the ferricenium ion, $[Mn^{IV}{}_2O_2(o\text{-phen})_4]^{4+}$, $[Co^{III}(o\text{-phen})_3]^{3+}$ and $[Ir^{IV}Cl_6]^{2-}$ [112].

c. Oxidation of O_2^- to $^1O_2$: Singlet oxygen, $^1O_2$, has been reported to originate through the disproportionation of $O^{2-\bullet}$ in the presence of a proton as well as from the oxidation of $O^{2-\bullet}$ with ferricenium ion and diacyl peroxides [113].

d. Role of oxidant *via* H-atom transfer from reducing agent: Since O_2^{2-} species is unstable in aprotic environments, the direct transfer of an electron to $O_2^{\bullet-}$ is an implausible procedure. As a result, most $O_2^{\bullet-}$ oxidations in these media actually represent the initial proton abstraction that produces the substrate anion and the species that follow disproportionation, HO_2^- and O_2. The latter oxidize the anion in the substrate. In this manner, the reducing substrates with easily exchangeable hydrogen atoms, such as dihydrophenazines, reduced flavins,

hydrazines and hydroxylamine (both models for reduced flavin) are oxidized by $O_2^{-\bullet}$ to produce, respectively, phenazine and N-methylphenazine radical.

e. Precursor in synthesis for new dioxygen complexes: The interaction of O_2 with a low-valent metal ion or complex is the most popular method for creating dioxygen complexes. It has also been possible to create dioxygen complexes of the elements Rh(I), Pd(II) and Al(III) using superoxide anions.

f. Intermediate in metal auto-oxidation reactions: A product or intermediate in metal ion catalyzed auto-oxidation reactions has been proposed as $O_2^{-\bullet}$. For instance, it has been demonstrated that the ions of Ag, Hg, Cd, Co, Pb and Zn generate $O_2^{-\bullet}$ in aqueous solution [114].

g. Non-oxidizing properties: A wide range of functional groups, including benzaldehyde in aprotic fluids, exhibit the oxidative inertness of $O_2^{-\bullet}$ [115]. The $O_2^{-\bullet}$ is thermodynamically unable to oxidize catechols or their anions in acetonitrile, according to voltammetric investigations. A proton transfer from 3,5-di-*t*-butylcatechol to $O_2^{-\bullet}$ followed by further chemistry with the resultant HO_2 species appears to be the initial stage of the reaction between the two substances. Presumably, initial proton transfer to O_2^- also occurs in the observed oxidations of hydrazines, thiols and alcohols.

h. Effective basicity: The $O_2^{-\bullet}$ exhibits a basic character in solutions by adsorbing a proton from substrates or solvents [116]. The combination of the reduction half-reaction for $O_2^{-\bullet}$ in water [117] and the reaction of O_2/O_2^- in water [118] results in the net expression of proton abstraction by superoxide, despite the fact that $HO_2^{\bullet}$ has a pK_a value of 4.88 (indicating that $O_2^{-\bullet}$ is a weak base) [118].

$$O_2^{\bullet-} + H_2O + e^- \rightleftharpoons HO_2^- + OH^-;\ E = +0.17\ V\ vs.\ NHE$$

$$O_2 + e^- \rightleftharpoons O_2^{\bullet-};\qquad E = -0.50\ V\ vs.\ NHE$$

$$2O_2^{\bullet-} + H_2O \rightleftharpoons O_2 + HO_2^- + OH^-;\qquad k = 2.5 \times 10^5$$

In fact, recent investigations have shown that $O_2^{-\bullet}$ ions deprotonate weakly acidic organic molecules like benzaldehyde in aprotic organic solvents. However, protic elements in impure benzaldehyde quickly deplete O_2 by reaction.

$$2O_2^{\bullet-} + HB \longrightarrow O_2 + HO_2^- + B^-$$

This is then followed by an aldehyde loss. Benzyl alcohol and an oxidized benzaldehyde species are the end products of this benzaldehyde and oxygen reaction, which is a Cannizzaro-type reaction [119]. Whether B^- is OH^- or HO_2^-, the end result is benzoic acid and benzyl alcohol.

$O_2^{-\bullet}$ is a highly reactive oxidizing agent that, by creating severe oxidative stress, has the power to seriously damage biological components like DNA [120], proteins [121] and lipids [122]. $O_2^{-\bullet}$ also has negative effects by interfering with iron-sulfur cluster-containing enzymes and rendering them inactive. The Fenton reaction occurs when this free iron is subsequently released into the cell, where it creates the incredibly reactive hydroxyl radical. Protonated HO_2^- form $O_2^{-\bullet}$ can also cause the lipid peroxidation of PUFAs. When it reacts with carbonyl molecules and halogenated carbon compounds, toxic peroxy radicals are also created. The $O_2^{-\bullet}$ production in tissues has effects that aren't always bad; on occasion, they even save lives. Activated phagocytes are able to produce significant amounts of $O_2^{-\bullet}$ [123,124], despite the fact that only tiny amounts of $O_2^{-\bullet}$ are produced in biological systems during the ordinary catalytic function of a number of enzymes or during the oxidation of haemoglobin to methemoglobin [125]. Most patients with chronic granulomatous disease, a genetic syndrome in which phagocytes cannot create oxygen, are fatal before the age of 10 [126], are particularly susceptible to bacterial and fungal infections. To form $O_2^{-\bullet}$ anion, leukocyte NADPH oxidase [127], an enzyme connected to the membrane of phagocyte cells, reduces oxygen by one electron. Because they can diminish potentially dangerous semiquinone molecules formed during a metabolic activity, a little amount of intracellular $O_2^{-\bullet}$ is very important [128,129]. The oxidative destruction of microorganisms is further aided by the oxidizing radicals generated by the $O_2^{-\bullet}$ in the Haber-Weiss and associated reactions.

$$O_2^- + Q^{\bullet} \longrightarrow O_2 + QH_2$$

Any interference in this detoxification of such semiquinones due to a lower $O_2^{-\bullet}$ concentration has been proposed as the basis harmful effects of too much superoxide dismutase. over the last few years it has become clear that both $O_2^{-\bullet}$ and H_2O_2 play crucial roles by being signalling molecules, changing the behaviour of proteins as diverse as transcription factors and membrane receptors by converting -SH groups of proteins to disulfide bonds and changing the oxidation states of enzyme-associated transition metals [130].

Reaction mechanisms of free radical: Most of the radicals are highly reactive due to their tendency to pair up the electrons and thus the radicals are powerful one electron redox reagents. The mechanism of these redox reactions put emphasis on the realization that how and by which steps one atom or group of atoms or the electron has transferred between two substrates.

Chemical reactions that are associated with any kind of electron transfer from one substrate to another and thus undergoing change in oxidation states of the reactants are called redox reactions. In such reactions transfer of one or more electron in a concerted or multistep process to the electron deprived oxidant from a reductant with prosperous amount of electrons. The electron transfer may proceed with or without a net chemical change with minimum rearrangement of atoms/groups around the central atom.

$$[Fe^{III}(CN)_6]^{3-} + [{}^*Fe^{II}(CN)_6]^{4-} \longrightarrow [Fe^{II}(CN)_6]^{4-} + [{}^*Fe^{III}(CN)_6]^{3-} \quad (1)$$

They may also be associated with atom/group transfer like oxygen transfer reactions, *e.g.*

$$2HCrO_4^- + 3H_3CCHO + 8H^+ \longrightarrow 3H_3CCOOH + 2Cr^{3+} + 5H_2O \quad (2)$$

Electron transfer reactions of transition metal complxes in homogeneous phase is divided into two broad mechanistic classes: Outer-sphere electron-transfer-reactions and Inner-sphere electron reactions.

Outer-sphere reactions: In outer-sphere-reactions electron transfer occurs with minimum electronic interaction *via* chemical bonding [131]. For pathways involving bridged intermediate the reaction undergoes outer sphere mechanism only when the

bridge is insulated and electron is actually transmitted through space as in the case of the complex shown below where Co^{III} reduced by Ru^{II}. Some of the examples of outer-sphere reaction are given in Table-3.

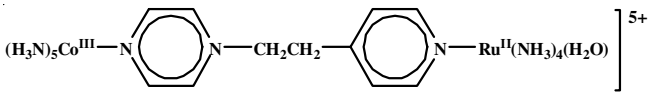


TABLE-3
EXAMPLES OF OUTER-SPHERE REACTIONS

Oxidant	Reductant	Ref.
$[Fe(CN)_6]^{3-}$ (a)	$[W(CN)_8]^{4-}$ (a)	[131]
$[Mo(CN)_8]^{3-}$ (a)	$[W(CN)_8]^{4-}$ (a)	[131]
$[IrCl_6]^{2-}$ (a)	$[Fe(CN)_6]^{4-}$ (a)	[131]
$[Fe(H_2O)_6]^{3+}$ (a)	$[Ru(NH_3)_6]^{2+}$ (a)	[132]
$[Co(phen)_3]^{3+}$(a)	$[V(H_2O)_6]^{2+}$ (a)	[133,134]
$[Co(H_2O)_6]^{3+}$(a)	$[Ni^{II}$cyclam]	[135]
$[IrCl_6]^{2-}$	$S_2O_3^{2-}$	[136]
$[Co^{III}(N_5)(HnPO_4)]^{n+}$	$[Fe(CN)_6]^{4-}$ (a)	[137]
[RuIII(edta)(pyz)]$^-$	L-ascorbic acid	[138]
trans-$[Ru(tmc)O_2]^{2+}$	I^-	[139]
$[Co(RNH_2)_5(H_2O)]^{3+}$	$[Fe(CN)_6]^{4-}$ (a)	[140]
$[Ni^{IV}$oxime$]^{4+}$	$[Fe(H_2O)_6]^{2+}$	[141]

According to Elding *et al.* [142] reduction of oral anticancer prodrugs *cis, trans*, *cis*-$[PtCl_2(OAc)_2(Cha)(NH_3)]$ and *cis, trans, cis*-$[PtCl_2(OCOC_3H_7)_2(Cha)(NH_3)]$ (Fig. 1) by ascorbate follow an outer-sphere pathway.

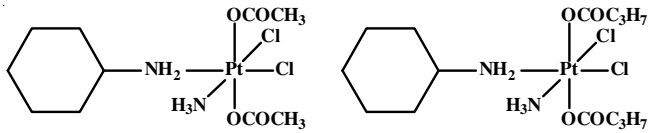
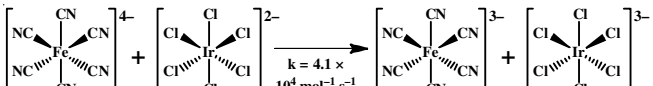


Fig. 1. *cis, trans, cis*-$[PtCl_2(OAc)_2(Cha)(NH_3)]$ *cis, trans, cis*-$[PtCl_2(OCOC_3H_7)_2(Cha)(NH_3)]$

When the rate of ligand exchange for both species is substantially slower than the rate of electron transfer, the mechanism is assured to be the correct one [143].



Outer-sphere reaction follows the steps as shown below:

Step-1: Formation of precursor complex:

$$Ox + Red \underset{}{\overset{K_A}{\rightleftharpoons}} \{Ox \parallel Red\}$$

Step-2: Activation of precursor complex and electron transfer:

$$\{Ox \parallel Red\}^* \overset{K_d}{\rightleftharpoons} \{Ox^- \parallel Red^+\}$$

Step-3: Dissociation to products:

$$\{Ox^- \parallel Red^+\} \rightleftharpoons Ox^- + Red^+$$

The overall reaction rate will be $k_{obs} = K_A K_{el}$

The free energy associated with the activation of the precursor (eqn. 3) complex may be expressed as a sum of three terms:

$$\Delta G^{\#} = \Delta G_1^{\#} + \Delta G_2^{\#} + \Delta G_o^{\#} \quad (3)$$

where $\Delta G_1^{\#}$ = free energy required to bring the oxidant and reductant into a configuration in which they are separate by a requisite distances (for charged reductants this includes work to overcome the columbic repulsion).

$\Delta G_2^{\#}$ = free energy required for bond compression and stretching to achieve orbital of equal energy.

$\Delta G_o^{\#}$ = free energy needed for solvent reorganization outside the first coordinated sphere.

The Frank-Condon principle [144] states that because internuclear distances and nuclear velocities are constant throughout the actual electron transfer, the transition state's ability to change its spin and angular momentum is constrained. By proposing that the electron transfer takes place at the intersection of two potential energy surfaces, one for the reactant (precursor complex) and the other for the product, this is incorporated into the conventional electron transfer theories (successor complex). When the orbital energies of the two become equal, electron transfer takes place at the intersection of potential energy surfaces. The magnitude of this interaction is correlated with the value of E in Fig. 2a. Small bond distortions result in high coupling interaction and advantageous electron transport. The interaction in the potential energy diagram is very weak and the reaction will be sluggish, if the free energy term $\Delta G^{\#}$ or substantial bond distortion, is present. These points also hold true for the heteronuclear reactions as shown in Fig. 2b.

Outer-sphere reaction and Marcus cross-relation: In order to explain the rates of electron transfer processes, in which an electron is transferred from one chemical species (electron donor) to another (electron acceptor), known as Marcus theory. When an electron is transferred between two chemical species, there are only minor structural changes and a change in charge (such as when an ion like Fe^{2+}/Fe^{3+} is oxidized). These reactions are known as outer sphere electron transfer reactions. Marcus created a framework in which the nuclear configuration changes of reactants, products and solvent molecules may be used to represent the electron-transfer rate constant. A thermodynamic cycle is generated, which can determine the amount of energy needed to reorganize the solvent molecules from their initial (equilibrium) state to one that is polarized out of equilibrium. Two different types of polarization, including orientation polarization and atomic and electronic polarization, are caused by the movement of atoms and electrons within solvent molecules in the direction of the field of charges. The rate of the reaction is consequently determined by the solvent polarization's free energy of activation. The equilibrium constant k_{AB} and the symmetry exchange rates k_{AA} and k_{BB}) for each redox pair, where A and B are chemical species and the asterisk represents an isotopic variation, can be used to predict the rate constant (k_{AB}) for asymmetric electron exchange in an outer-sphere reaction [145].

$$A^+ + B \rightarrow A + B^-$$

$$A^- + A^* \rightarrow A + A^{-*}$$

$$B^- + B^* \rightarrow B + B^{-*}$$

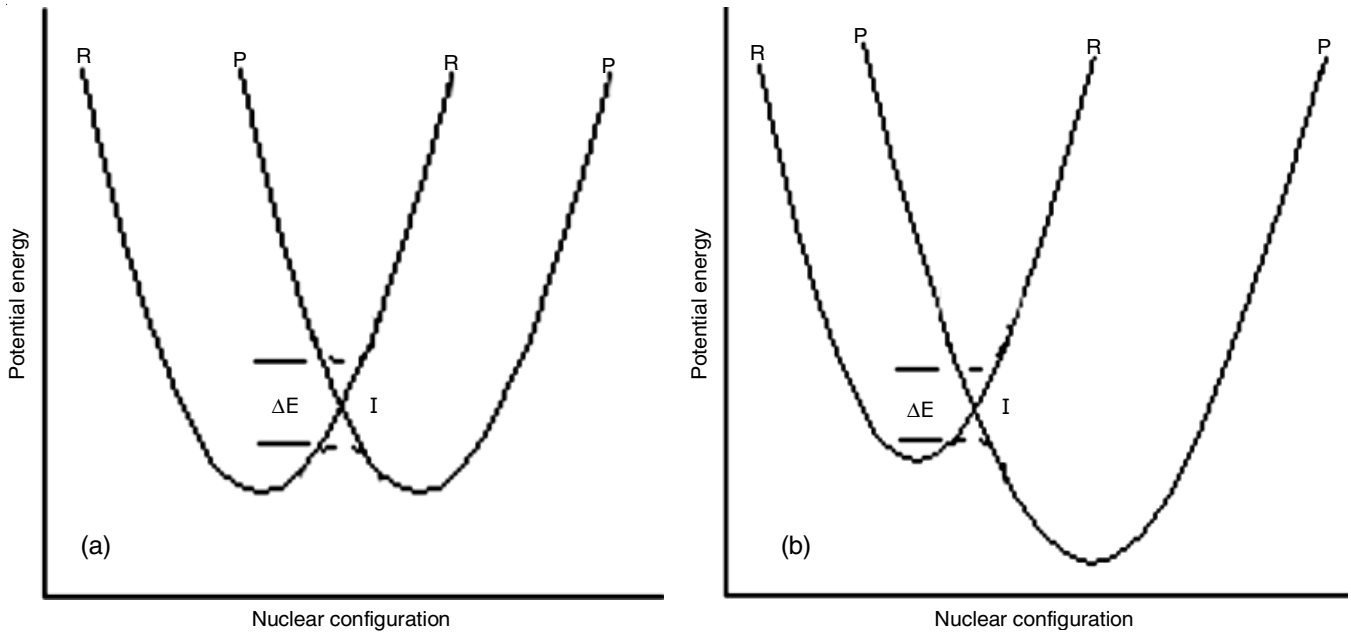


Fig. 2. Intersection of potential energy surfaces

Marcus reorganized certain simplifications that led to the cross-relationship.

$$k_{AB} = (k_{AA}k_{BB}K_{AB}f_{AB})^{1/2} \quad (4)$$

where, log $f_{AB} = (\log K_{AB})^2/\{4\log(k_{AA}k_{BB}/Z^2)\}$ and Z is the collision number (~1011 M^{-1} s^{-1}) for the ions in solution. The factor $f_{AB} \approx 1$ unless K_{AB} is large. If $f_{AB} \approx 1$, eqn. 4 simplifies to the eqn. 5, called the simplified Mercus equation:

$$k_{AB} = (k_{AA}k_{BB}K_{AB})^{1/2} \quad (5)$$

At 25 ºC for one electron transfer, the logarithmic form of the above mentioned relation is,

$$\log k_{AB} = 0.5 (\log k_{AA} + \log k_{BB}) + 8.46E^o \quad (6)$$

where Eº is the standard E.M.F. of the cross-reaction at 25 ºC.

Thus, if series of releated reactions with $f_{AB} \sim 1$ is studied as a function of driving force (Eº), a plot of log k_{AB} *versus* Eº should be linear, with slope 0.5 and an intercept 0.5 (log k_{AA} + log k_{BB}). For example, reduction of polypyridineiron(III) complexes by Fe^{2+}_{aq} [146] and cerium(IV) oxidation of polypyridine iron(II) complexes [147], the observed slope (0.51) is close to the expected value (0.5), but the intercepts are smaller than predicted.

Sutin *et al*. [134] reviewed these applications and found that Marcus theory can typically accurately estimate the outer-sphere electron transfer rate constants between +2 and +3 charged reactants to within a factor of 25. Comparison of some rate constants were compared from the Marcus cross relationship are shown in Table-4.

Ion pairing, on the other hand, is likely the single biggest obstacle to the accurate use of the Marcus model for reactions of charged species in solution [151]. Numerous published works presumably contain unrecognized references to ion pairing. In many of these instances, discrepancies between the experimental and calculated numbers sparked in-depth debate. Rarely has simple ion pairing been suggested as the origin of this disparity. The recommended reviews by Wherland [152] and Swaddle [153], who have both made significant experimental contributions in this field, discuss the effects of ion pairing. In addition, Marcus [154] and Saveant [155] provided evidence of the significance of ion pairing in electron transfer reactions. For the O_2/O_2^- pair (1103 M^{-1} s^{-1}), Taube *et al*. [156] determined the self-exchange rate constant of three Ru(II) ammine complexes. Espenson *et al*. [157] improved the approach by incorporating work terms to account for asymmetries in the charge and size of the species involved. They estimated the prior study using more reducing agents.

Eqn. 7 provides the Marcus relation with the work term.

$$k_{AB} = (k_{AA}k_{BB}K_{AB}f_{AB})^{1/2}W_{AB} \quad (7)$$

TABLE-4
COMPARISON OF SOME OBSERVED RATE CONSTANTS (M^{-1} s^{-1}, 25.0 ºC) [148] WITH THOSE CALCULATED FROM THE MARCUS CROSS-RELATIONSHIP [149,150]

Reaction	k_{12} (M^{-1} s^{-1})	
	Observed	Calculated
$[IrC1_6]^{2-} + [W(CN)_8]^{4-}$	6.1×10^7	6.1×10^7
$[Mo(CN)_8]^{3-} + [W(CN)_8]^{4-}$	5.0×10^6	4.8×10^6
$[Fe(CN)_6]^{3-} + [W(CN)_8]^{4-}$	4.3×10^4	6.3×10^4
$Ce^{IV} + [W(CN)_8]^{4-}$	$> 10^8$	4.0×10^8
L-Co[(-)PDT A $]^{2-} + [Fe(bipy)_3]^{3+}$	8.1×10^4	$> 10^5$
L-Fe[(-)PDTA]$^{2-}$ + [Co(EDTA)]$^-$	1.3×10^1	1.3×10^1
Fe[(-)PDTA]$^{2-}$ + $[Co(ox)_3]^{3-}$	2.2×10^2	1.0×10^3
$[Cr(EDT A)]^{2-} + [Co(EDTA)]^-$	$\approx 3.0\times10^5$	4.0×10^7
$[Fe(EDTA)]^{2-} + [Mn(CyDTA)]^-$	$\approx 4.0\times10^5$	6.0×10^6
$[Co(EDTA)]^{2-} + [Mn(CyDTA)]^-$	9.0×10^{-1}	2.1
$[Co(terpy)_2]^{2+} + [Co(bipy)_3]^{3+}$	6.4x10	3.2x10
$[Fe(phen)_3]^{2+} + [MnO_4]^?$	6.0×10^3	4.0×10^3
$[Fe(CN)_6]^{4?} + [MnO_4]^?$	1.3×10^4	5.0×10^3
$[V(H_2O)_6]^{2+} + [Ru(NH_3)_6]^{3+}$	1.5×10^3	4.2×10^3
$[Ru(en)_3]^{2+} + [Fe(H_2O)_6]^{3+}$	8.4×10^4	4.2×10^5

where, f_{AB} and W_{AB} are given by $\ln f_{AB} = [\ln K_{AB} + (w_{AB} - w_{BA})/RT]2/\{4\ln (k_{AA}k_{BB}/Z^2) + (w_{AA} + w_{BB})/RT\}$ and $W_{AB} = \exp\{-(w_{AB} + w_{BA} - w_{AA} - w_{BB})/2RT\}$, respectively.

The individual work terms are calculated from

$$W_{ij} = \frac{4.23 Z_A Z_B}{r(1+0.328rI^{½})} \quad (8)$$

where, r is the radii of the reaction partners in E, I is the ionic strength, the numerical constants are for water at 25 ºC and W_{ij} are in kcal mol^{-1}.

Only when a diverse variety of driving forces and charge types are involved in the reactions are the f factor and work terms taken into account. f_{AB} approaches unity when G°_{AB}, the reaction's overall free energy, is close to zero (*i.e.*, $K_{AB} \approx 1$).

There was no direct method to measure the self exchange rate of various metalloenzymes. The only tool in these situations is Marcus cross-relation, however difficulties are typically attributable to different angles of enzyme attack and consequent conformational changes in the enzyme [158].

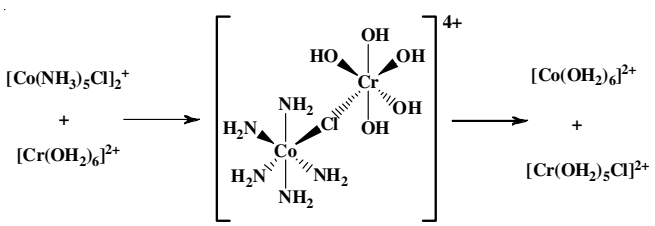
The Marcus relation is unable to account for changes in anharmonicity, the type of coordinated ligands surrounding the central metal ion, multiplicity differences in the solution of the hydrophobic/hydrophilic reactants and changes in the mechanism [159-166]. Marcus relation is now regularly used to verify the validity of the proposed outer-sphere paths [147, 167-182] and to calculate rates of reactions which are otherwise difficult to measure [147,170,171]. To obtain unknown redox potential Marcus cross-relation plays an important role using K_{AB} which is found from rate data [168,169]. If the redox partners are sterically inhibited, outer-sphere electron transport may require more activation than predicted from the Marcus relation [183]. Non-coulombic interaction, hydrogen-bonding, change in mechanism is not considered in the Marcus theory.

Electronic configuration and rate of electron transfer: Electron gain or loss changes the electronic configuration of a species. For metal complexes, this change is accompanied by a change in metal-ligand and intra-ligand bond lengths and angles as well as changes in the vibrations and orientations of the surrounding solvent dipoles. According to Frank-Condon principle [144], the rate constants for electron transfer reactions depend on the difference in the electronic configuration of the reactants and products; the smaller the difference, the faster is the reaction. For example, self-exchange rate increases in the order, $[Fe(CN)_6]^{3-/4-} < [Fe(H_2O)_6]^{3+/2+} < [Cr(H_2O)_6]^{3+/2+}$, which is the order of increasing difference of metal-ligand bond length between a redox partners. Self exchange rate for $[V(H_2O)_6]^{2+}$ (t_{2g}^3) [$k = 1.7 \times 10^{-2}$ s^{-1}] is higher than $[Cr(H_2O)_6]^{2+}$ ($t_{2g}^3e_g^1$). Thermodynamically electron transfer from Cr^{II} to Cr^{III} is favourable as electron goes from anti-bonding level but severe bond length change occurs. But in case of $[V(H_2O)_6]^{3+}$ anti-bonding level not affected and therefore changes in its metal-ligand distances are small. The nature of the bound ligand has a significant influence on the reaction rate. For $[Co(phen)_3]^{3+/2+}$ self exchange rate is higher than $[Co(NH_3)_6]^{3+/2+}$ [184]. This is due to π-electron cloud of ligand phenanthroline which provides easy passage of electrons. Similar trends were also observed with non-metallic redox couples [185-190]. For example, the couples $S_2O_3^{2-}/S_2O_3^{-}$, I^-/I, SCN^-/SCN, N_3^-/N_3 all have very high self-exchange rates [189]. The unpaired electron in $S_2O_3^-$, SCN, N_3 and I resides in a non-bonding molecular orbital. Hence, small change in geometry and small structural reorganization, limited to the solvent sphere, are expected during oxidation to these species. One-electron oxidation of NO_2^- and SO_3^{2-} involves an electron in π* and σ* orbital, respectively. Removal of the anti-bonding electron increases the bond angle from 115º to 134º in NO_2^-/NO_2 couple and from 106º to 111º in the SO_3^{2-}/SO_3^- (estimated from ESR data) [186-188]. The large structural changes result in low self-exchange rates, 1.0×10^{-2} M^{-1} s^{-1} for NO_2^-/NO_2 couple [185] and 4.0 M^{-1} s^{-1} for the SO_3^{2-}/SO_3^- couple [190]. The couple NH_2OH/NH_2OH^+ has a record low self exchange rate due to the huge structural reorganization that occurs when the tetrahedral nitrogen in NH_2OH becomes planar on oxidation. Same things also expected for $N_2H_4/N_2H_4^+$ couple (≤ 0.3 M^{-1} s^{-1}).

Marcus relation cannot explain change in the nature of coordinated ligands around central metal ion, change in multiplicity differences in the solution of hydrophobic/hydrophilic reactants, anharmonicity and a change in the mechanism [164]. Instead of shortcomings this theory is the only tool for measuring self exchange rate of various enzymes in which cases no other direct methods could be applied, but the difficulties usually being attributed to varying point of attack on the enzyme and included conformational change in the enzyme [191].

Marcus relation is now regularly used to verify the validity of the proposed outer-sphere paths [167-171] and to calculate rates of reactions which are otherwise difficult to measure [168,170,171]. To obtain unknown redox potential Marcus cross-relation plays an important role using k_{AB} which is found from rate data [167,192]. Outer-sphere electron transfer may require greater activation than anticipated from Marcus relation, if the redox partner is sterically hindered. Non-coulombic interaction, hydrogen-bonding, changes in mechanism are not considered in the Marcus theory.

Inner sphere electron transfer reaction: Simultaneous bond breaking and making along with electron transfer makes inner sphere electron transfer more completed with respect to outer sphere pathway. The electron gets transferred to the oxidant from the reductant *via* a bridging group which both the reactants share as ligand in their primary coordination sphere. The rate of the reaction cannot be faster than the rate of exchange of the ligand in the absence of a redox reaction as ligand exchange is an intimate part of the process.



The above reaction is the classic example of this mechanism [193]. The chloride atom, firmly attached to the inert Co^{III} ion can rapidly displace a water molecule from labile Cr^{II} complex

to form a bridged intermediate, $[(NH_3)_5Co\text{-}Cl\text{-}Cr(OH_2)_5]^{4+}$. Electron transfer occurs within this dinuclear complex leading to the formation of reduced Co^{II} and oxidized Cr^{III}. The intermediate species dissociates in to chloroaqua complex of Cr^{III} and five coordinated cobalt(II) species, which immediately hydrolyzes to Co^{2+}.

The presence of bridging ligand is vital for inner-sphere mechanism. Changes in the bridge accompany changes of redox rates by many orders of magnitude. Presence of an unshared electron pair in the coordinated ligand appears a minimum requirement for the ligand to be a potential bridging group, for it has to function as a Lewis base towards two metal cations.

The bridged intermediate with the shared ligand is named the precursor complex if its electronic configuration is closer to that of the reactants [194] and is called successor complex if its electronic configuration resembles that of the product. Electron transfer across the bridging ligand can be depicted by two extreme mechanisms. In one, a radical is produced *via* electron transfer from the metal ion of the reducing agent to the bridging ligand. Consequential electron transfer from radical ion to the metal ion of the oxidizing agent occursnext [195]. This is often called the radical or stepwise mechanism. In the second type the bridge acts simply as a mediator of electron flow. This is known as tunneling mechanism.

Bridging ligand in inner-sphere redox reactions: The presence of bridging ligand is vital for inner-sphere mechanism. Changes in the bridge accompany changes of redox rates by many orders of magnitude. This has been well exhibited considering the reaction as shown below:

$$Cr^{2+} + [Co(NH_3)_5L]^{n+} + 5\ H^+ \rightarrow [CrL]^{n+} + Co^{2+} + 5\ NH_4^+ \quad (9)$$

Examination of data for eqn. 9 in Tables 5 and 6 show that there is some general order of reactivity for the various ligands L. Presence of an unshared electron pair in the coordinated ligand L appears a minimum requirement for L to be a potential bridging group, for it has to function as a Lewis base towards two metal cations. Thus $[Co(NH_3)_6]^{3+}$ and $[Co(NH_3)_5py]^{3+}$ oxidize Cr^{2+} by an outer-sphere mechanism giving Cr^{3+} as the product, at much slower rate than that by $[Co(NH_3)_5H_2O]^{3+}$.

TABLE-5
RATE CONSTANTS (k, $M^{-1}\ s^{-1}$) FOR THE REDUCTION OF $[Co(NH_3)_5L]^{n+}$ HAVING DIFFERENT BRIDGING LIGANDS, T = 25°C [196]

L	Cr^{2+}
NH_3	8.0×10^{-5}
Py	4.1×10^{-3}
H_2O	≤ 0.01
I^-	3×10^6
N_3^-	3×10^5
OH^-	1.5×10^6

TABLE-6
EFFECT OF DIFFERENT BRIDGING LIGANDS ON RATES OF Cr(II)-Cr(III) EXCHANGE REACTIONS, T = 25 °C [196]

Exchange partners	k ($M^{-1}\ s^{-1}$)
$Cr^{2+} + Cr^{3+}$	$\leq 2 \times 10^{-5}$
$Cr^{2+} + [CrOH]^{2+}$	0.7
$Cr^{2+} + CrSCN$	40
$Cr^{2+} + cis\text{-}[Cr(N_3)_2]^+$	60

From the studied reactions, Cr^{2+}-$[CrX]^{2+}$, Cr^{2+}-$[Co(NH_3)_5X]^{2+}$ and Eu^{2+}-$[Cr(H_2O)_5X]^{2+}$, it seems to be that electron transfer is associated with the polarizability of bridging ligand as the rates decreases as X is varied in the order $I^- > Br^- > Cl^- > F^-$ [197]. However, the opposite order is found for Fe^{2+}-$[Co(NH_3)_5X]^{2+}$ and Eu^{2+}-$[Co(NH_3)_5X]^{2+}$ reactions thus showing that the order is not simply a function of ion used [198].

When a polyatomic bridging ligand in the oxidant presents more than one potential donor site towards the reducing metal ion, remote and adjacent attack is a possibility. An authentic example of this kind as reported by Haim & Sutin [199], $[Cr(H_2O)_6]^{2+}$ can attack nitrogen end in the oxidant $[Co(NH_3)_5SCN]^{3+}$ and reduction proceeds with a rate constant $1.9 \times 10^{-5}\ M^{-1}\ s^{-1}$. Alternatively, the reductant can attack at the sulfur atom directly bound to Co^{III} and the observed rate is then $8 \times 10^{-4}\ M^{-1}\ s^{-1}$ [199]. When the reducing agent is the soft $[Co(CN)_5]^{3-}$ ion only remote attack on soft S atom takes place [200].

$$[(NH_3)_5CoSCN]^{2+} + Cr^{2+} \longrightarrow [(NH_3)_5CoSCNCr]^{4+} \quad (10)$$

$$[(NH_3)_5CoSCNCr]^{4+} + 5H^+ \longrightarrow [CrNCS]^{2+} + Co^{2+} + 5\ NH_4^+ \quad (11)$$

$$[(NH_3)_5CoSCN]^{2+} + Cr^{2+} \longrightarrow [(NH_3)_5CoS(Cr)CN]^{4+} \quad (12)$$

$$[(NH_3)_5CoS(Cr)CN]^{4+} + 5H^+ \longrightarrow [CrSCN]^{2+} + Co^{2+} + 5\ NH_4^+ \quad (13)$$

$$[(NH_3)_5CoNCS]^{2+} + [Co(CN)_5]^{3-} \longrightarrow [(CN)_5CoSCN]^{3-} + Co^{2+} + 5\ NH_4^+ \quad (14)$$

With azide ion as bridge, a remote attack has generally been assumed [201-204]. Snellgroove & King [201] suggested a double bridged transition state in the reduction of *cis*-$[Cr(H_2O)_4(N_3)_2]^+$ by Cr^{2+}. In the reaction between $[Co(EDTA)]^-$ and Cr^{2+}, three oxygen atoms of EDTA evidently serve as bridges [197].

Intimate mechanism: The mechanism of electron transfer across the bridging ligand is of immense importance and two extreme mechanisms can be proposed. In one, a radical anion is created when an electron is transported from the metal ion of the reducing agent to the bridging ligand. Subsequently, the electron is transferred from radical ion to the metal ion of the oxidizing agent [195,205]. This is often called the chemical, radical or stepwise mechanism. In other mechanism, the resonance or exchange mechanism, the bridge acts simply as a mediator of electron flow. This is known as tunneling mechanism. The relative reduction rates of Co^{III} and Cr^{III} with simple bridges (F^-, Cl^-, CH_3COO^-) are widely different. This can be explained by the fact that reductions of Co^{III} and Cr^{III} through simpler bridges such as Cl^- occur by the concerted σ-orbital path, since these species are not reducible as it is unfavourable energetically. On the other hand, isonicotinamide complexes of Co^{III} and Cr^{III} are reduced at very similar rates. One explanation for this is that the bridges [206-209] such as isonicotinamide are reducible and itself isonicotinamide is a delocalized, extended bond system and reductions proceeding through such bridges occur by a chemical or radical mechanism. After precursor formation, the first step is Cr^{II} activation followed by transfer of an electron into a π*-orbital of isonicotinamide. This generate

Cr^{III} and the radical anion, $H_2NCOC_5H_4N^-$ which were detected and supports the free radical nature of the bridges [209,210].

Bridging ligands play two different roles in inner-sphere mechanisms. It facilitates the transport of the electron (kinetic contribution) and brings the metal ions together (thermodynamic contribution) [211]. The kinetic contribution results from elements like oxidant-reductant rearrangement and matching of the donor and receptor MO involved, whereas the thermodynamic contribution results from elements crucial to the stability of the intermediate complex. Studies of inner-sphere reactions involving organic bridging ligands are very fascinating and instructive because they demonstrate how the steric effects in the bridge, the point at which the reductant attacks the bridge and the electronic structure of the bridge, including its reducibility, can all affect reaction rates [212].

Mixed outer- and inner-sphere reactions: In some reactions, outer- and inner-sphere operate simultaneously [213-216]. An interesting example of this behaviour is the reaction of $[Cr(H_2O)_6]^{2+}$ with $[IrCl_6]^{2-}$ which has been studied and well-understood [217].

$$[Cr(H_2O)_6]^{2+} + [IrCl_6]^{2-} \xrightarrow{71\%} [Cr(H_2O)_6]^{3+} + [IrCl_6]^{3-} \quad (15)$$

$$[Cr(H_2O)_6]^{2+} + [IrCl_6]^{2-} \xrightarrow{21\%} [(H_2O)_5CrClIrCl_5] \quad (16)$$

$$[(H_2O)_5CrClIrCl_5] \xrightarrow{39\%} [Cr(H_2O)_6]^{3+} + [IrCl_6]^{3-} \quad (17)$$

$$[(H_2O)_5CrClIrCl_5] \xrightarrow{61\%} [Cr(H_2O)_5Cl]^{2+} + [IrCl_6H_2O]^{2-} \quad (18)$$

The majority of the reaction at 0 ºC happens through an outer-sphere mechanism. A binuclear complex used in the residual inner-sphere process is capable of undergoing both Cr-Cl and Ir-Cl cleavage.

Using the Marcus equation, it is possible to calculate the outer-sphere rate constant for the $[Cr(H_2O)_6]^{2+}/[IrCl_6]^{2-}$ reaction as 109 M^{-1} s^{-1}. With the very labile $[Cr(H_2O)_6]^{2+}$ ion (d^4), a value of this magnitude can undoubtedly compete with that for the inner-sphere path [217]. Additionally, Marusak *et al.* [216] reported the parallel pathways of an inner-sphere pathway leading to $[Cr(en)_2ox]^+$ and an outer-sphere pathway leading to $[Cr(en)_3]^{3+}$ are used to reduce $[Co(ox)_3]^{3-}$ (d^6, inert) by the labile $[Cr(en)_3]^{2+}$ (d^4).

According to a recent publication [218], noradrenaline [4-(2-amino-1-hydroxyethyl)benzene-1,2-diol] interacts with $[Fe(OH)]^{2+}$ in anaerobic acid solution to produce iron(II) and the semiquinone form of noradrenaline, which is then quickly oxidized by additional iron(III) to produce noradrenoquinone. The reaction is an illustration of parallel electron transmission between the inner and outer spheres.

Multiple electron transfer: When the formal oxidation state of oxidant or reductant changes by more than one unit, multiple electron transfer occur. Reactions (eqn. 19) and (eqn. 20) are the examples, where overall two electron transfers take place. Photosynthesis water oxidation is a four electron transfer reaction [159].

$$Hg^0 + Tl^{III} \longrightarrow Hg^{II} + T^{II} \quad (19)$$

$$Pt^* + Pt^{IV} \longrightarrow Pt^{IV*} + Pt^{II} \quad (20)$$

$$2H_2O \longrightarrow 4H^+ + O_2 + 4e \quad (21)$$

Reactions in which the formal oxidation states of the oxidant and reductant both change by the same number of units are called complementary reaction, for example

$$Sn^{II} + Tl^{III} \longrightarrow Sn^{IV} + T^{I} \quad (22)$$

$$Sn^{II} + Hg^{II} \longrightarrow Sn^{IV} + Hg^0 \quad (23)$$

In a non-complementary reaction [219,220], the oxidation states of the reactants change by unequal amounts and the stoichiometries are not 1:1, for example

$$2Fe^{II} + Tl^{III} \longrightarrow 2Fe^{III} + T^{I} \quad (24)$$

Some of the best examples of non-complementary processes in transition metal chemistry are chromate ion oxidation. In this process, each of the three elementary steps [221-223] involves a single electron-transfer.

$$Cr^{IV} + Red \longrightarrow Cr^{V} + Ox \quad (25)$$

$$Cr^{V} + Red \longrightarrow Cr^{IV} + Ox \quad (26)$$

$$Cr^{IV} + Red \longrightarrow Cr^{III} + Ox \quad (27)$$

Low probability for simultaneous transfer of two or more electrons due to the strong Franck-Condon barrier for simultaneous multi-electron transfer, there is a low chance for simultaneous transfer of two or more electrons [224]. More than two electrons, two electrons and then one electron form the barrier. Going from a one-electron to a comparable two-electron system results in a rate decrease of just a factor of 2 to 4 according to theory for gas phase reactions, which indicates that the barrier between two and one electron-transfer is not overly great [225]. However, it has been proposed that the $Tl^{I/III}$ exchange and the oxidation of Hg_2^{II} by Tl^{III} both include two electron transfers. The outer shell barrier is four times higher for a two-electron transfer than it is for a one-electron transfer and the exchange entails a significant change in the length of the metal-oxygen bond. These elements support the one-electron transfer process with Tl^{II} serving as the intermediary. $Tl^{I/III}$ exchange is an actual two-electron transfer mechanism because the equilibrium constant for the production of Tl^{II} is so unfavourable (eqns. 10-33) that it is eight orders of magnitude slower than the reported rate [226,227]. The sequence is suggested by the Hg_2^{II}/Tl^{III} reaction rate law.

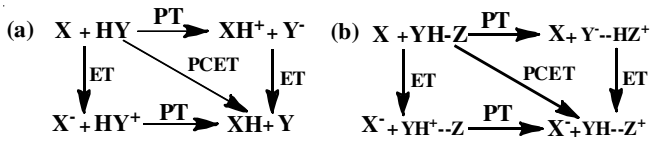
$$Hg_2^{II} \rightleftharpoons Hg^{II} + Hg^0 \quad (28)$$

$$Hg^0 + Tl^{III} \longrightarrow Hg^{II} + T^{I} \quad (29)$$

Di-nuclear complexes appeared to be more prone to two-electron transfer processes. When the driving power for electron transfer from a multi-electron donor is insufficient to produce free radicals, a mechanism involving two electron acceptors is required. For instance, the rate law for the reduction of $Fe^{III}P$ by ascorbic acid in [228] includes a $[Fe^{III}P]^{2-}$ term, revealing the active species to be the Fe^{III}-P dimer. Two-electron transfer has a low energy pathway thanks to the creation of Fe^{III}-P dimers.

Proton coupled electron transfer (PCET): In addition to the previously outlined process, radicals also participate in some reactions where the redox phenomena involves the coupled transfer of electrons and protons from an initial state to a final state. In other words, the "function" of the electron transfer is the proton transfer. Coupled electron and proton transfer can occur over two rival routes. It can be a consecutive process with electron transfer (ET) followed by proton transfer (PT). The slash indicates that this process is sequential and referred to as ET/PT.

In general, a chemical reaction involving the transfer of an electron and a proton can proceed either *via* concerted pathways without an intermediate or by stepwise pathways including initial electron transfer (ET) or initial proton transfer (PT). Proton-coupled electron transfer (PCET) is the name given to the coordinated mechanism [229]. **Scheme-I** serves as an example of this notion, where the horizontal lines denote proton transfer (PT) and the vertical lines denote electron transfer (ET). The diagonal process is PCET. In contrast, stepwise routes involve an intermediate step in addition to mechanistically different ET and PT phases.



Scheme-I

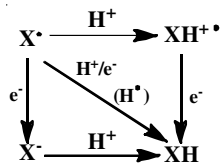
The stepwise procedures in the square schemes correspond to travelling around the square's edges. The PCET processes [230] are stepwise reactions where ET and PT occur at comparable rates and/or cannot be separated kinetically, but such coupling can be addressed by conventional kinetic treatments [229].

Hydrogen atom transfer (HAT) and other concerted electron/proton transfers are both included in the definition of PCET. A hydrogen atom moving between groups X and Y is what is commonly meant when someone uses the acronym HAT as shown in the diagonal of **Scheme-IA**. The PCET reactions can also occur when the proton and electron are split in some way in the reactants, products or transition state. One instance of such a non-HAT process is proton transfer across the hydrogen bond when electron transfer from a hydrogen-bonded YH-Z unit is coupled to it as shown in **Scheme-IB**. The PCET is more frequently used to refer to coordinated proton/electron transfer that is not HAT. However, it can be challenging to draw this distinction, particularly when metals are involved.

However, as the lifespan of the intermediate reduces to outside the detection limit, the distinction between one-step HAT and sequential ET/PT becomes murky. No intermediate would be found if quick PT followed by ET served as the rate-determining step. No deuterium kinetic isotope effect (KIE) would be seen in such a scenario. This should be contrasted from one-step HAT, which typically displays deuterium kinetic isotope effects despite the absence of intermediates. Although the absence of ET intermediates gives good evidence for the sequential ET/PT processes, this does not necessarily entail that the reaction proceeds in a single step using HAT [231].

Knowing the thermochemistry of each stage is crucial for determining whether a reaction follows a concerted or sequential course. Redox potentials (E) and pK_a values, respectively, describe the thermodynamics of electron transfer and proton transfer reactions. Both parameters have a connection to measurements of free energy (G^o). Bond dissociation energies (BDEs, bond strengths), which are measures of enthalpies (H^o), are frequently used in discussions of HAT processes. BDEs are not heavily influenced by temperature or the solvent, but they have a less direct relationship with rate constants (which are related to free energies of activation *via* transition state theory). Since $S^o = 0$, the G^o and H^o for a HAT reaction XH + Y > X + HY are often relatively near (for reactions accompanied by minor changes in solvation). The E and pK_a measurements taken in solutions allowed for the precise determination of bond strengths. A square scheme (**Scheme-II**) for a single reagent has a diagonal whose energy is equal to the sum of the energies of two steps around the square that lead to the same point. There are two of these two-step routes and their energies must be equal:

$$2.3RTpK_a(XH) + nFE(X^{\bullet}/X^{-}) = nFE(XH^{\bullet+}/XH) + 2.3\ RTpK_a(XH^{\bullet+})$$



Scheme-II

The presence of a pH-dependent term in the rate law for $[Fe(H_2O)_6]^{3+}/[Fe(H_2O)_6]^{2+}$ self-exchange reaction investigated by isotopic labelling appears to have been the first recorded indication of PCET as mechanism. A route involving $[Fe^{II}(H_2O)_6]^{2+}$ and $[Fe^{III}(H_2O)_5(OH)]^{2+}$ that occurred with $k(H_2O)/k(D_2O) \approx 2$ and was attributed to "H-atom transfer" from $[FeII(H_2O)_6]^{2+}$ to $[FeIII(H_2O)_5(OH)]^{2+}$ was found to increase in rate with rising pH [232]. Thorp published a succinct review of PCET in excited states and metal complexes in 1991 [233] and 1996 [234], respectively. In the middle of 1990s, Cukier [235] and Hammes-Schiffer & Fang [236] reported a number of theoretical studies. Cukier & Nocera [237] published a review on PCET in 1998, while Babcock & Hoganson [238] published a number of groundbreaking articles on the coupling of electron and proton transport in photosystem II and other enzymes in the mid- to late 1990s [238]. Recent brief reviews on the PCET's theoretical [239,240] and experimental [241] features have also been published. Reviews on the use of density functional theory to study redox enzymes, such as PCET, have also been published [242].

Recent publications [243-245] have demonstrated that the radical-scavenging reactions of phenolic antioxidants, such as vitamin E (α-tocopherol) and flavonoids, happen either by an electron transfer followed by a proton transfer or by a hydrogen atom transfer from the phenolic OH group. Galvinoxyl radical (GO•) and cumyl peroxyl radical are scavenged by (+)-catechin

in aprotic media like acetonitrile and propionitrile *via* an electron transfer from (+)-catechin to the radicals, followed by a proton transfer (which is significantly speed up by the presence of metal ions like Mg^{2+} and Sc^{3+}). According to the reactants and the surroundings, at least three distinct pathways [246] can be used for the reactions of phenol with free radicals that entail the abstraction of the hydroxylic hydrogen ($R^{\bullet}$+ ArOHArO$^{\bullet}$ + RH):

i. HAT (hydrogen atom transfer)
ii. PCET (proton-coupled electron transfer)
iii.SPLET (sequential proton-loss electron transfer) route.

Both the HAT and PCET methods can be referred to as "single-event electron transfers with atom transfers" and only require one reaction step (no reaction intermediates) [247]. However, the aforementioned reaction is preceded by the formation of an ArOH...R$^{\bullet}$ hydrogen-bonded complex when R$^{\bullet}$ has an unshared pair of electrons [248]. The SPLET process involves more than one kinetic reaction step, in contrast to both the HAT and PCET systems [249]. Understanding the connection between the HAT and PCET mechanism is essential [240] for a wide range of reactions. The PCET mechanism, which uses amino acid radical intermediates, is used in the case of many enzyme redox processes to produce radical reactions [250]. Photosystem II [238], DNA photolyase [251], cytochrome oxidases [252] and ribonucleotide reductase (RNR) [253] reactions are a few significant examples. The knowledge of single electron transport in proteins has been greatly aided by the Marcus theory and results from model systems [254] and PCET has to be added to this set of resources. Although it is a common misconception, the intramolecular oxidation of tyrosine by Ru^{III}, which takes place through a covalent linkage of Ru-Tyr [255], followed by the deprotonation from tyrosine [256], defies this notion.

Redox properties of radical: The majority of radical-related redox reactions do not happen by straightforward outer-sphere electron transfer pathways. Redox processes exclusively use outer sphere mechanisms when minor bond rearrangements are not necessary. After the electron transfer, the majority of the uncharged radicals will become charged substances and as a result, they will have a significantly larger solvation energy than the uncharged species at first. For instance, in case of H^+ or OH^- the redox products of H or OH radicals, have low hydration energies, they have large solvation energies. On the other hand, the reduced form of $^{\bullet}H$, H^-, is unstable and needs a subsequent reaction with H^+ to generate H_2 in order to continue. Organic radicals have a carbon core and a lot of oxidizing and reducing power. The kind of substitution on the carbon determines the redox characteristics of aliphatic carbon-centered radicals. For instance, radicals of the type $^{\bullet}CR_1R_2(OH)$ are capable of oxidizing low-valent transition metal complexes like $[Cr(H_2O)_6]^{2+}$ and $[V(H_2O)_6]^{2+}$ but are nonetheless relatively potent reductants. Alkyl-peroxyl radicals and CH_2CO_2H, on the other hand, are relatively potent oxidizing agents. These types of compounds do not frequently undergo outer sphere reactions since the self exchange rates for the cationic and anionic radical couples are usually slow and the products are extremely unstable. However, because these radicals are potent reducing agents and their oxidation does not necessitate significant bond rearrangements, outer-sphere reductions of transition metal complexes by $^{\bullet}CR_1R_2OH$ or $^{\bullet}CR_1R_2O^-$ radicals were also observed [257]. An intriguing illustration of an inner sphere reaction is $[Fe(Phen)_3]_3$ oxidation +'s of alkyl radicals ($^{\bullet}CH_3$). The addition of an alkyl radical to the phenanthroline ligand may be thought of as starting the reaction, followed by an electron transfer to the metal *via* the bridge and then a proton loss from the phenanthroline ligand [258]. It has long been believed that superoxide radicals are immediately transformed into O_2 by outer-sphere electron transfer to transition-metal complexes. The fact that these mechanisms follow the Marcus model for outer-sphere electron transmission is evidence in favour of them. In fact, the Marcus model is followed by the oxidation of hydroquinones and phenols as well as the reduction reaction caused by the superoxide radical [259,260].

Metal bound radicals: Not only the study of free radical chemistry but also the study of chemistry of metal-bound radical complexes is a major research aim in the field of homogeneous catalysis and enzymatic reactions at the active site of different metalloenzymes.

The coordination chemistry of transition metals with ligands like nitroxidedithiadiazolyl [261], semiquinone [262], tetracyanoethylene (TCNE) [263], tetracyanoquinodimethane (TCNQ) [264], verdazyl [265], derivatives of tetrathiafulvalenyl [266] and diphenylcarben [267] radicals have been studied for their redox activity in metal coordinated state. Above mentioned many radicals behave as a catalyst either by themselves [268] or in combination with transition metals [269]. Neutral radical ligands, like phenoxyls [270] play a great role as redox active ligand in the catalytic chemistry of galactose oxidase [19].

Characteristics of metal bound redox active radical ligands: Redox active ligands that are bound to metals typically go through bonding with the metal and/or have an extended-system. During the oxidation or reduction of the complex, they are able to delocalize the accumulated charges and unpaired spin density. Such complexes necessitate a thorough investigation in order to determine the genuine (spectroscopic) oxidation states of the metal (*d*-electron configuration) and/or the ligands (ligand electron configuration). The actual "spectroscopic oxidation state" that is acquired may be very different from the declared oxidation state. To underline the ambiguity in oxidation states in such circumstances, the phrase "ligand redox non-innocence" is employed [271]. In many cases, the presence of discrete and substantial spin density at a ligand fragment results in completely different reactivity patterns than commonly observed for these ligands in diamagnetic, closed-shell complexes. This phenomenon is known as "ligand redox non-innocence," which leads to the formation of radical ligands. In these circumstances, the ligands frequently turn into the most reactive site of the complex and can go through selective reactions, which is significantly different from the uncontrolled reactivity of free radicals. Since the metal and ligand centres share the electron spin density, which results in more stability of the radical ligands, this is energetically possible. These redox ligands' non-innocence features considerably alter their reactivity patterns and

open the door to swift, precise and targeted radical-type organometallic reactions [272].

Examples of metal bound radical complexes: Few known and well studied organometallic compounds which bear radical ligands are discussed below:

Metal-alkene radical complex: The alkene ligands that receive ions may not be'redox innocent. Alkene ligands can accept (part of) the unpaired electron(s) from the transition metal to its π* orbitals, generating a carbon-centered radical, when they are coordinated to paramagnetic transition metals. One-electron activated cots (cot = cyclooctatetraene) coordinated to Fe [273], Ru [274], Co [275] or Rh [276] have undergone a thorough investigation into their chemistry, which has shown that they are capable of radical-type C-C bond formation processes.

Metal-carbene radical complex: Group VI transition metals are reduced by one electron using external reducing agents like Na/K alloy and SmI_2 to produce Fischer-type carbene complexes. These complexes' LUMO is located on the carbon of the carbene, giving the ligands their typical electrophilic nature. When these complexes are reduced by one electron, the existence of this LUMO allows carbon-cantered "carbene-radicals" to form [277,278]. These carbon-cantered radicals could be used in processes that produce carbon-carbon bonds. The tungsten diphenylmethylsilylmethoxycarbene is an example of such a compound.

Metal-phenoxyl radical complex: Since the stability of uncoordinated phenoxyl radical ligands is often low, the metal-phenoxyl radical complexes were produced by one-electron oxidation of the metal-phenolate complexes. By chemical and photochemically oxidizing iron(III)-phenolate complexes, Wieghardt *et al.* [204] reported the first discovery of the phenoxyl radical complexes. The absorption peaks at 400 and 600 nm that are observed in the metal-coordinated phenoxyl radical are attributed to the phenoxyl radical's π–π* transition [279, 280]. The Cu(II) and Ni(II) phenoxyl radical complexes are two examples.

Metal-amino acid radical complex: Amino acid radicals typically form during enzyme catalysis, which is now well-known [94]. Enzymes that include amino acid radicals are frequently associated with transition metal ions like manganese, iron, cobalt or copper. According to reports, redox-active organic co-factors like S-adenosylmethionine or flavins can sometimes take the place of the metal. Tyrosine-based radical enzymes are among the most extensively documented types [270]. The fungal enzymes galactose oxidase, amine oxidase, cytochrome c oxidase, *etc.* are more examples of enzymes that use tyrosine residues and metals as partners to effect redox chemistry.

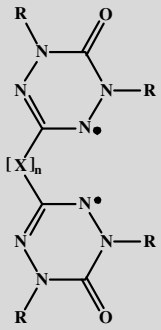
Metal-porphyrin π-cationic radical complex: The extensive involvement of metalloporphyrin-cation radicals as intermediates in biological systems containing haem proteins like catalases and peroxidases. The electronic structure of metalloporphyrin is altered by the interaction between the unpaired electrons in iron and the porphyrin ring, which changes the magnetic character. In the case of *meso*-substituted complexes, an electron is taken from the porphyrin a_{2u} HOMO during the one electron oxidation of Fe(III) porphyrins, which typically results in Fe(III) porphyrin radical cations [281]. The Fe(III) porphyrin radical cations should have a wide range of electronic ground states since the Fe(III) ion has different spin-states and electron configurations. A low spin Ni(II) porphyrin was synthesized after cooling to 77 K, demonstrating intramolecular electron transport and another metal-porphyrin cationic radical complex, similar to Ni(II) porphyrin-cation radical, was synthesized at ambient temperature [282].

Applications of metal bound free radical complexes: In coordination chemistry and homogeneous catalysis, one of the "hot subjects" at the moment is the ligand-centered reactivity of transition metal complexes with "cooperative" and "redox-active" ligands [283]. Over the past few years, there has been a lot of interest in ligands that can support catalytic transformations by holding and releasing one or more electrons during catalytic turnover [284]. Due of the associated ligand-centered redox processes seen in various metalloenzymatic reactions, ligands' "redox non innocent" behaviour has drawn more attention [285]. As a result, several effective and commercially relevant "bio-inspired" catalytic reactions have been developed [286]. Molecular magnetism can be seen in a large number of transition metal complexes containing organic free radicals as a ligand. One of the most promising methods for obtaining a variety of magnetic metal-organic compounds is the so-called "metal-radical approach" [287]. The organic ligands' open shell structure strengthens the magnetic exchange interactions brought on by the direct overlap of metal and radical magnetic orbitals. Table-7 displays a few radical species as examples.

Metal bound superoxo complex: A number of intermediates are produced by stepwise reduction of molecular oxygen linked to metal centres. Early oxygen activation results in the formation of mononuclear superoxide and peroxo (including hydroperoxo) species, which either act as active oxidants or are precursors to more reactive species [289]. Various superoxo, hydroperoxo and high valentoxo complexes that are formed by transition metals have been chemically and spectroscopically described. Another example can be found in biological systems, where superoxo coupled to iron(III) heme is created at the various biological oxygen carriers' reaction centres in oxygen-rich environments [290]. Superoxo radical is a potent nucleophile and in the absence of straightforward breakdown pathways, can form quite robust metal complexes. Other less persistent superoxo complexes of d^0-metal ions are also known [291], in addition to the transition metal superoxo complexes mentioned above that have substitution inert centres. Transition metal superoxo complexes are significant because many homogeneous catalytic redox processes are thought to involve them as essential intermediates [292]. Metals such as Ni(II), Zn(II), Co(II), Co(III), Fe(II), Fe(III), Ce(III), Cr(III), Ti(IV) and Mo are known to occur in superoxo complexes (VI). Binuclear (coordinated) superoxo compounds are typically easier to prepare and can frequently be kept in their crystallized condition throughout storage. The majority of mechanistic studies [293,294] use transition metal-bound oxo or superoxo complexes to oxidize organic substrates, however there are very few trustworthy quantitative studies [295] that address their reactivity. Even

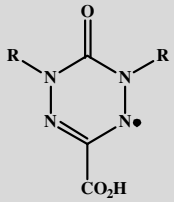
TABLE-7
STRUCTURES OF SOME RADICALS AND METAL-RADICAL COMPLEXES

Verdazyl radicals useful as ligand



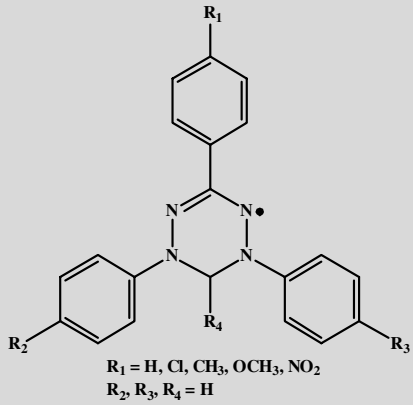
A

X = N-donor heterocyclic compound



B

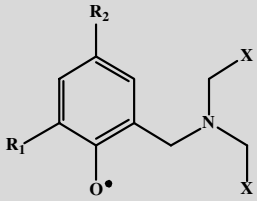
A water-soluble verdazyl (redox reagent)



C

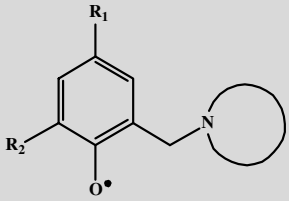
Another examples

Phenoxyl radicals with chelating arm



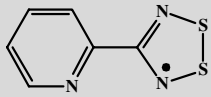
D

X = N-donor heterocyclic compound



E

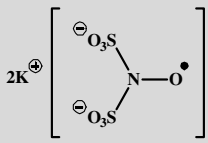
Aza-oxa or azamacrocyclic arm



F

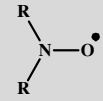
4-(2'-Pyridyl)-1,2,3,5-dithiadiazolyl radical

Fremy's salt



G

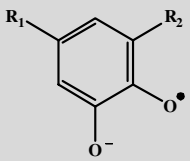
Long known member of the nitroxide family



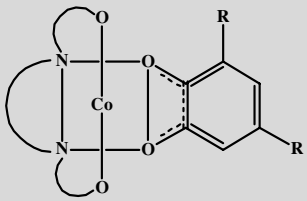
H

It is an useful reagent for many selective organic oxidations [Ref. 288]

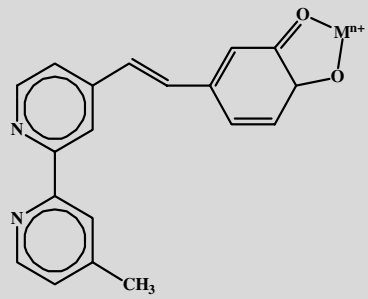
Semiquinones



I

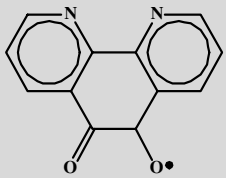


J



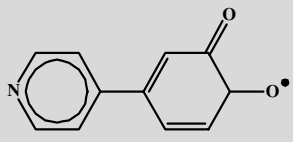
K

Metal-semiquinones with chelating arm



L

Binecleating semiquinone

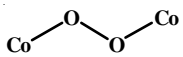


M

Semiquinone with remote basic site

though a thorough mechanistic analysis of the chemistry of hydrocarbon auto-oxidation has yielded useful knowledge about the reactivity of organic intermediates like carbon or oxygen radicals toward various substrates, much less is known about the reactivity of various inorganic intermediates towards organic ones [296]. Thus, the interaction of various metal superoxo complexes with acyl or peroxyl radicals yields useful data.

Characterization of complexes: Characterization of the metal-dioxygen complex and their bonding mode is important as they can be taken as a model for dioxygen binding proteins, especially haemoglobin and myoglobin [297]. Paramagnetic species include both mono- and binuclear metal superoxo compounds. Generally binuclear metal superoxo complexes they have equivalent metal atoms and the unpaired electron reside primarily on the bridging O_2^- group. Mainly they have been shown to be staggered. *i.e.*



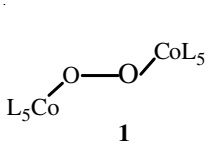
Similar near-coplanarity exists between the superoxo group and metal atoms. The superoxide oxygen-oxygen bond is viewed by Paulings as combining a single (σ) bond with a three electron (π) bond. It is difficult for this anion to produce any other type of bridging compound other than a planar one since two of the orbitals are used in the formation of O-O bond. The oxygen atoms in the superoxo bridge are never engaged in any hydrogen bonding, as was discovered from the crystal structures. Superoxide (O_2^-) groups coordinated to metal centres are now easier to find and characterize because to the use of Raman and infrared spectroscopy techniques [298]. The superoxo group of the dicobalt-superoxo complex exhibits an O-O bond with an IR stretching frequency of close to 1100 cm^{-1}. The Raman spectra show a fairly strong resonance peak at 1120.10 cm^{-1} and a relatively faint resonance at 1075.5 cm^{-1} for the O_2^- group, respectively, for analogous monobridged and di-bridged-superox-dicobalt complexes. A second hydroxo or amido bridge significantly reduces the intensity of O_2^{2-}-stretching frequency [299]. Assignments of the structure of the former complexes based only on an O-O stretch may be incorrect because di-bridged complexes exhibit significantly weaker and generally wider Raman bands than mono-bridged complexes.

Reaction of metal bound μ-superoxo complexes: The involvement of this anion in metabolic processes has sparked intense interest in reactions of metal-bound superoxide complex. The reduction of metal-bound superoxo and peroxo complexes by metal ions like Cr^{2+} and V^{2+} was previously explored [300, 301]. It was proposed that the superoxo complex is reduced through an outer-sphere process [302]. Reactions at low pH with the metal centre reductants Fe^{2+}, Cr^{2+}, V^{2+} and Eu^{2+} as well as with the dimeric species $Mo_2O_4^{2+}$ have been the focus of the redox chemistry of metal superoxide complexes [303]. Each time, the dimeric-peroxocation is reduced by $1e^-$ and eventually breaks down into a metal ion and oxygen throughout the reaction. Numerous investigations into the electron transfer processes involving different reducing agents and oxo-bridging cobalt(III) complexes have conclusively shown that the reduction takes place at the bridged dioxygen rather than the metal centre [304]. Similar to this, the palladium superoxo complex is extremely reactive and capable of oxidizing simple alkenes into epoxide [305]. The reduction of the superoxide functional group that results from a reaction with SO_2 and SO_3^{2-} is accompanied by the integration of the oxidation product, SO_4^{2-}, into the coordination sphere of metal. Studies are also being done on the interactions of bonded superoxide with non-metallic reductants like hydrazine, hydroxylamine, ascorbate and azide [306].

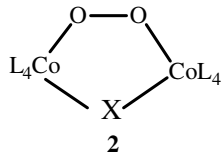
Mono and dibridged cobalt(III)-superoxo complex: Studies of monobridged, μ-superoxo-*bis*[pentaamminecobalt(III)]pentachloride and dibridged, μ-amido-μ-superoxo-*bis*[tetraamminecobalt(III)]tetranitrate complexes as the model radical complex continued to be useful since they are easy to prepare, store and handle under ambient reaction conditions.

Nature of superoxo bridge: Structure of this two compound has been elucidated by the application of ESR [307] and crystal X-ray data [308] both of which supports the fact that both of the cobalt atoms are equivalent each with a oxidation state of +3 and in both complex the unpaired electron resides primarily on the bridging O_2 group.

The cobalt(III)-superoxo complex can take on the monobridged (**1**) or dibridged (**2**) forms, as shown below:



1



2

Here, L represents the neutral (NH_3 and ethylene diamine, en) ligands and X represents the anionic bridging ligands (NH_2^- and OH^-) [299].

The monobridged-superoxo-*bis*[pentaamminecobalt(III)]$^{5+}$ ion's CoOOCo atoms are connected by normal bonds, according to Marsh and Schaefer's X-ray studies [308] and complex has a *trans* configuration (**1**). The oxygen bridge of di-bridged μ-amido-μ-superoxo-*bis*[tetraamminecobalt(III)]$^{4+}$ ion is in a *cis*-configuration as opposed to the single bridged complex (**2**). The covalent bonds that hold the di-oxygen bridge to the cobalt atoms are strong, well-defined and durable [309]. The cobalt (3*d*) orbital interacts with the oxygen (2*p*) orbital to form the link.

The monobridged complex have the Co-O and O-O bond lengths as 189.4 and 1.31 Å, respectively and the Co-O-O angle is 118º. The dibridged complex has little difference that the O-O bond length is little longer by 0.01 Å (1.32 Å) and also the Co-O-O angle is wider by 2º (120º) [310]. The O-O distance in both of the complex is close to the O-O distance (1.28 Å) in KO_2 [311].

In the first complex, the four atoms Co-O-O-Co and in the second complex the ring of five atoms Co-O-O-Co-X (X = hydroxo or amido) are found to be nearly coplanar [312]. The five-membered ring has a sum of angle of 539.6º which has adisparity of small angle of 0.4º from the expected value. In this ring of second complex, two of the oxygen atoms are in a line that is on the opposite and 0.045 Å away from the Co-N-Co plane.

Nature of superoxo bridge: The measured ESR spectra show that both compounds contain a superoxo bridge, that

the unpaired electron is delocalized over the bridge and that it interacts equally with the nuclear spins of terminal cobalt atoms. Weil & Kinnaired's [313] experiments on these compounds with the addition of ^{17}O to the bridge show that the unpaired electron is located over the Co-O-O-Co atoms in a molecular orbital, with the nodal plane being parallel to the plane made by the atoms or in the case of a dibridged complex, the ring. A unpaired electron (S = 1/2) is further supported by magnetic susceptibility studies in the μ-superoxo bridge [314].

The two cobalt atoms' equal contributions to the nuclear hyperfine structure shown in the EPR spectra have confirmed the total equivalency of the two cobalt atoms in these mono and di-bridged complexes [315]. The only significant difference between the EPR spectra of the mono- and di-bridged metal-superoxide complex solutions is the degree of resolution of the 15-line cobalt hyperfine structure [307]. Additionally, it suggests that the electron is not only delocalized over nearby cobalt orbitals by means of the link. The formulation of the superoxo bridge is also consistent with other elements of the EPR data [316]. The Raman stretching frequency for the O_2^- group, as was mentioned earlier, clearly shows the existence of the superoxo bridge. For this group, the resonance ranges for the monobridged and dibridged complexes are 1120 cm^{-1} and 1075 cm^{-1}, respectively. Due to the lower intensity of the O_2^{2-} stretch frequency, the di-bridged complex may be distinguished from the single bridged one [299].

The UV-VIS optical spectra of superoxo complexes show three of four transitions between 250 and 1000 nm which are due to the presence of *d-d* transitions involving changes in spin multiplicity. The single bridged complex shows peaks at ~ 670 nm (ε = 850 ± 40 M^{-1} cm^{-1}), ~ 480 nm (ε = 270 ± 20 M^{-1} cm^{-1}), ~ 345 nm (ε = 1200 ± 600 M^{-1} cm^{-1}) and ~ 297 nm (ε = 24500 ± 1500 M^{-1} cm^{-1}). The peak that arises in far UV range at 297 nm actually arises due to the transfer of unpaired lone electron from the superoxo bridge to either of the two cobalt atoms [317,318]. For the di-bridged complex the main peak at ~ 700 nm in the visible range gives the complex its blue-green colour.

The difference in geometry of the O_2^- bridge in the mono and di-bridged complexes are believed to be an important factor in the determining of the magnitude of entropy of activation because difference in structures may provide altered steric hindrance to the approaching reducing agent.

Reactions of cobalt μ-superoxo complexes: Reagents with a lower oxidation potential than 1.1 volts (such as those involved in reactions with Br^- and VO^{2+}) are typically used to decrease the dicobaltsuperoxo complexes with amine ligands. Iodide [319] reduces the μ-superoxo-*bis*[pentacyanocobalt(III)] complex in the acidic solutions and the following examples indicate potential stoichiometry and products:

$$Co^{III}O_2 - Co^{III} \xrightarrow{e^-} Co^{III}O_2^{2-}Co^{III}$$

$$Co^{III}O_2 - Co^{III} \xrightarrow{3e^-} 2Co^{III} + 2H_2O$$

$$Co^{III}O_2 - Co^{III} \xrightarrow{4e^-} Co^{III} + H_2O + Co^{II}$$

$$Co^{III}O_2 - Co^{III} \xrightarrow{5e^-} 2Co^{II} + H_2O$$

In absence of the intramolecular redox reaction:

$$Co^{III}O_2^{2-} - Co^{III} \longrightarrow 2Co^{II} + O_2$$

The limiting diffusion current is found to correspond to a value of napp = 3, where napp is the apparent number of electrons transported by the electrode, in a variety of polarographic studies of the superoxo complexes at room temperature [320, 321]. When the temperature is lowered to zero degrees, napp falls to less than two, suggesting the creation of secondary products, one of which has virtually the same electrochemical potential as the superoxo complex and is electrochemically active. When superoxo complex is reduced in its initial stage in this reaction, oxygen is produced as a byproduct and is also reduced in the same potential region as the superoxo complex. With the creation of oxygen, the rate of breakdown of the initial products slows down in the following order: $Co(O_2)Co$ >> $Co(-NH_2,O_2)Co$.

Reduction of cobalt μ-amido-μ-superoxo complex proceeds rapidly with NO_2^-, N_2H_4, $[Fe(CN)_6]^{4-}$, AsO_2^- and $S_2O_3^{2-}$ but slowly or not at all with Hg^{2+} or $NH_2OH{\cdot}HCl$ [322]. When aqueous ammonia reduces $[(NH_3)_4Co(\mu\text{-}NH_2,O_2)Co(NH_3)_4]^{4+}$ the corresponding μ-amido-μ-peroxo complex is formed. The reaction of $[(NH_3)_4Co\text{-}\mu(NH_2,O_2){\cdot}Co(NH_3)_4]^{4+}$ is also reduced by excess aqueous ethyldiamine. Both cobalt superoxide complexes have characteristic peaks in the visible range (670 and 700 nm), so the one-electron reduction reaction can generally be studied without the interference from subsequent reactions by following the rate of decrease of absorbance under pseudo first-order conditions.

Metal ions (like Fe^{2+}) also reduce the superoxo complexes acid media at constant ionic strength. Since the metal atoms remain in same oxidation state (as cobalt(III) in products, these reactions are essentially one-equivalent reductions of di-oxygen bridge [313]. Hoffman & Taube [300] studied the reactions of V(II), Cr(II) and Eu(III) with $[(NH_3)_5Co(\mu\text{-}O_2)Co(NH_3)_5]^{5+}$ complex by using stopped-flow techniques. Intermediate of the reaction is $[(NH_3)_5CoO_2Co(NH_3)_5]^{4+}$ whichdecompose to Co(II) and O_2. All the reactions have been found to proceed through outer-sphere mechanism.

The reduction reaction of superoxo complexes by metal ion is catalyzed by a number of anions [323]. In case of the reaction with Fe(II) with $[(NH_3)_5Co(\mu\text{-}O_2)Co(NH_3)_5]^{5+}$ complex is catalyzed by different anions in the following order of their observed rate, k_{cat} value (M^{-1} s^{-1}): F^-(7000) > Cl^- (390) > SO_4^{2-} (193) > Br^- (84) >> NO_3 (0.28).

Reduction of $[(NH_3)_5Co(\mu\text{-}O_2)Co(NH_3)_5]^{5+}$complex with VO^{2+}, Sn^{2+}, $S_2O_3^{2-}$ and As(III) using OsO_4 as catalyst have been found to have a stoichiometry of 1:1 [324]. Reactions with sulphite and nitrite are also electron-transfer reactions but they show different stoichiometry and products along with a possibility of group transfer between the reactants. The mechanism shows that reactions proceed through the formation of ion-pairing between the complex and anion SO_3^{2-} or NO_2^-. Similar reactions with di-bridged complex $[(NH_3)_4Co(\mu\text{-}NH_2,O_2)\text{-}Co(NH_3)_4]^{4+}$ with SO_3^{2-} or NO_2^- shows more complex stoichiometric results. Oxidized products of both anion are potentially capable of forming bridges between Co(III) atoms [325].

Conclusion

In conclusion, it is undoubtly said that radicals are playing an important role to control the biological as well as chemical interest to the researchers in all fields. Specially, the metallo-superoxide has an major role to control the biological system in human body.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. A.L. Lavoisier, Traité élémentaire de chimie, Cuchet, Paris 1789, vol. 1, English Translation by R. Kerr, reprinted by Dover Press: New York (1965).
2. M. Gomberg, *J. Am. Chem. Soc.*, **23**, 109 (1901); https://doi.org/10.1021/ja02028a005
3. B. Halliwell and J.M.C. Gutteridge, Free Radicals in Biology and Medicine, Clarendon Press: Oxford, Edn. 2 (1999).
4. A. Ito, Y. Nakano, M. Urabe, T. Kato and K. Tanaka, *J. Am. Chem. Soc.*, **128**, 2948 (2006); https://doi.org/10.1021/ja056318e
5. G. Nagendrappa, *Resonance*, **10**, 72 (2005); https://doi.org/10.1007/BF02835925
6. L. Wojnarovits, *J. Chem. Educ.*, **88**, 1658 (2011); https://doi.org/10.1021/ed1011053
7. K. Bagchi and S. Puri, *East. Mediterr. Health J.*, **4**, 350 (1998); https://doi.org/10.26719/1998.4.2.350
8. D.H. Hey and W.A. Waters, *Chem. Rev.*, **21**, 169 (1937); https://doi.org/10.1021/cr60068a006
9. J.L. Redpath, *J. Chem. Educ.*, **58**, 131 (1981); https://doi.org/10.1021/ed058p131
10. S. Fukuzumi, K. Ohkubo and Y. Morimoto, *Phys. Chem. Chem. Phys.*, **14**, 8472 (2012); https://doi.org/10.1039/c2cp40459a
11. M. Gomberg, *J. Chem. Educ.*, **9**, 439 (1932); https://doi.org/10.1021/ed009p439
12. P.O.P. Ts'o, J.C. Barret, W.J. Csspary, S.A. Lesko, R.J. Lorentzen and L.M. Sehechtman, Eds.: K.C. Smith, Aging, Carcinogenesis and Radiation Biology, Plenum Press: New York and London (1976).
13. S. Licht, G.J. Gerfen and J. Stubbe, *Science*, **271**, 477 (1996); https://doi.org/10.1126/science.271.5248.477
14. R. Banerjee, *Chem. Rev.*, **103**, 2083 (2003); https://doi.org/10.1021/cr0204395
15. J. Knappe and A.F. Volker Wagner, *Adv. Protein Chem.*, **58**, 277 (2001); https://doi.org/10.1016/S0065-3233(01)58007-9
16. P. Dorlet, S.A. Seibold, G.T. Babcock, G.J. Gerfen, W.L. Smith, A.L. Tsai and S. Un, *Biochemistry*, **41**, 6107 (2002); https://doi.org/10.1021/bi015871f
17. J. Cheek and J.B. Broderick, *J. Am. Chem. Soc.*, **124**, 2860 (2002); https://doi.org/10.1021/ja017784g
18. O.T. Magnusson and P.A. Frey, *Biochemistry*, **41**, 1695 (2002); https://doi.org/10.1021/bi011947w
19. J.W. Whittaker, *Chem. Rev.*, **103**, 2347 (2003); https://doi.org/10.1021/cr020425z
20. R.M.J. Palmer, D.S. Ashton and S. Moncada, *Nature*, **333**, 664 (1988); https://doi.org/10.1038/333664a0
21. R.S. Sohal and R. Weindruch, *Science*, **128**, 379 (1996); https://doi.org/10.1126/science.273.5271.59
22. Y.Z. Fang and R.L. Zheng, Theory and Application of Free Radical Biology, Beijing Scientific Press, pp. 647 (2002).
23. Y.Z. Fang, Free Radicals and Nutrition, In: Theory and Application of Free Radical Biology, Beijing Scientific Press (2002).
24. D.L. Gilbert and N.Y. Ann, *Ann. N. Y. Acad. Sci.*, **899**, 1 (2000); https://doi.org/10.1111/j.1749-6632.2000.tb06172.x
25. Y.Z. Fang, C.P. Sun, X.H. Tian and J.-H. Cong, *Am. J. Chin. Med.*, **26**, 153 (1998); https://doi.org/10.1142/S0192415X98000208
26. G. Wu and C.J. Meininger, *Annu. Rev. Nutr.*, **22**, 61 (2002); https://doi.org/10.1146/annurev.nutr.22.110901.145329
27. M.J. Jackson, *Proc. Nutr. Soc.*, **58**, 1001 (1999); https://doi.org/10.1017/S0029665199001317
28. A. Phaniendra, D.B. Jestadi and L. Periyasamy, *Indian J. Clin. Biochem.*, **30**, 11 (2015); https://doi.org/10.1007/s12291-014-0446-0
29. Z. Haida and M. Hakiman, *Food Sci. Nutr.*, **7**, 1555 (2019); https://doi.org/10.1002/fsn3.1012
30. E.I. Stiefel, I. Bertini and H.B. Gray, Biological Inorganic Chemistry: Structure and Reactivity, University Science Books, California (2007).
31. R.G. Hicks, *Org. Biomol. Chem.*, **5**, 1321 (2007); https://doi.org/10.1039/b617142g
32. S. Lomnicki, H. Truong, E. Vejerano and B. Dellinger, *Environ. Sci. Technol.*, **42**, 4982 (2008); https://doi.org/10.1021/es071708h.
33. M. Abe, *Chem. Rev.*, **113**, 7011 (2013); https://doi.org/10.1021/cr400056a.
34. D.C. Nonhebel and J.C. Walton, Free-Radical Chemistry; Structure and Mechanism, Cambridge University Press (1974).
35. D. Griller and K.U. Ingold, *Acc. Chem. Res.*, **9**, 13 (1976); https://doi.org/10.1021/ar50097a003
36. E.M. Pliss, I.V. Tikhonov and A.I. Rusakov, Eds.: A. I. Kokorin, Nitroxides–Theory, Experiment and Applications, InTech, Rieka, pp. 263 (2012)
37. H. Rath, S. Tokuji, N. Aratani, K. Furukawa, J.M. Lim, D. Kim, H. Shinokubo and A. Osuka, *Angew. Chem. Int. Ed.*, **49**, 1489 (2010); https://doi.org/10.1002/anie.200906017
38. R.G. Hicks and K.U. Ingold, Eds.: R.G. Hicks, Stable Radicals: Fundamentals and Applied Aspects of Odd-Electron Compounds, John Wiley & Sons Ltd (2010).
39. K.H. Cheeseman and T.F. Slater, *Br. Med. Bull.*, **49**, 481 (1993); https://doi.org/10.1093/oxfordjournals.bmb.a072625
40. R.V. Lloyd, P.M. Hanna and R.P. Mason, *Free Radic. Biol. Med.*, **22**, 885 (1997); https://doi.org/10.1016/S0891-5849(96)00432-7
41. C. Schweitzer and R. Schmidt, *Chem. Rev.*, **103**, 1685 (2003); https://doi.org/10.1021/cr010371d
42. H. Karoui, N. Hogg, C. Frejaville, P. Tordo and B. Kalyanaraman, *J. Biol. Chem.*, **271**, 6000 (1996); https://doi.org/10.1074/jbc.271.11.6000
43. M.D.E. Forbes, Carbon-Centered Free Radicals and Radical Cations, Structure, Reactivity and Dynamics, John Wiley & Sons, Inc., Hoboken, New Jersey (2010).
44. B. Halliwell, Encyclopedia of Life Sciences, Nature Publishing Group (2001).
45. G.J. Blackwell and R.I. Flower, *Br. Med. Bull.*, **39**, 260 (1983); https://doi.org/10.1093/oxfordjournals.bmb.a071830
46. M. Tsuruga and K. Shikama, *Biochim. Biophys. Acta Protein Struct. Mol. Enzymol.*, **1337**, 96 (1997); https://doi.org/10.1016/S0167-4838(96)00156-2
47. F.S. Pala and K. Tabakçioglu, *Adv. Mol. Biol.*, **1**, 63 (2007).
48. K.A. Kelly, C.M. Havrilla, T.C. Brady, K.H. Abramo and E.D. Levin, *Environ. Health Perspect.*, **106**, 375 (1998); https://doi.org/10.1289/ehp.98106375
49. B.M. Babior, *J. Clin. Invest.*, **73**, 599 (1984); https://doi.org/10.1172/JCI111249
50. K. Asada and K. Kiso, *Eur. J. Biochem.*, **33**, 253 (1973); https://doi.org/10.1111/j.1432-1033.1973.tb02677.x
51. J.P. Kehrer, *Toxicology*, **149**, 43 (2000); https://doi.org/10.1016/S0300-483X(00)00231-6
52. B. Uttara, A.V. Singh, P. Zamboni and R.T. Mahajan, *Curr. Neuropharmacol.*, **7**, 65 (2009); https://doi.org/10.2174/157015909787602823
53. R. Ferrari, C. Ceconi, S. Curello, A. Cargnoni, E. Pasini, F. De Giuli and A. Albertini, *Am. J. Clin. Nutr.*, **53**, 215s (1991); https://doi.org/10.1093/ajcn/53.1.215s
54. L. Gianni, J.L. Zweier, A. Levy and C.E. Myers, *J. Biol. Chem.*, **260**, 6820 (1985); https://doi.org/10.1016/S0021-9258(18)88854-8
55. M. Narwaley, K. Michail, P. Arvadia and A.G. Siraki, *Chem. Res. Toxicol.*, **24**, 1031 (2011); https://doi.org/10.1021/tx200016h

56. C. Sonntag, Free radical induced DNA damage and its Repair: A Chemical Perspective, Springer (2006).
57. D.F. Church and W.A. Pryor, *Environ. Health Perspect.*, **64**, 111 (1985); https://doi.org/10.1289/ehp.8564111
58. C.J.A. Doelman, R. Leurs, W.C. Oosterom and A. Bast, *Exp. Lung Res.*, **16**, 41 (1990); https://doi.org/10.3109/01902149009064698
59. J.R. Kanofsky and P. Sima, *J. Biol. Chem.*, **266**, 9039 (1991); https://doi.org/10.1016/S0021-9258(18)31548-5
60. R. Atkinson, *Atmos. Environ.*, **34**, 2063 (2000); https://doi.org/10.1016/S1352-2310(99)00460-4
61. W.B. DeMore, S.P. Sander, D.M. Golden, R.F. Hampson, M.J. Kurylo, C.J. Howard, A.R. Ravishankara, C.E. Kolb and M. Molina, Chemical Kinetics and Photochemical Data for Use in Stratospheric Modeling, Evaluation No. 12, JPL Publ. (1997).
62. R. Atkinson and J. Arey, *Chem. Rev.*, **103**, 4605 (2003); https://doi.org/10.1021/cr0206420
63. C.S. Foote, J.S. Valentine, A. Greenberg and J.F. Liebman, Active Oxygen in Chemistry, Chapman and Hall: New York (1985).
64. J.J. Steinberg, J.L. Gleeson and D. Gil, *Arch. Environ. Health*, **45**, 80 (1990); https://doi.org/10.1080/00039896.1990.9935930
65. K.B. Storey, Functional Metabolism: Regulation and Adaptation, Wiley-Liss, Inc. (2004).
66. B. Halliwell and J.M.C. Gutteridge, *FEBS Lett.*, **307**, 108 (1992); https://doi.org/10.1016/0014-5793(92)80911-Y
67. A. Kunwar and K.I. Priyadarsini, *J. Med. Appl. Sci.*, **1**, 53 (2011).
68. J.S. Beckman and W.H. Koppenol, *Am. J. Physiol. Cell Physiol.*, **271**, C1424 (1996); https://doi.org/10.1152/ajpcell.1996.271.5.C1424
69. E. Madej, L.K. Folkes, P. Wardman, G. Czapski and S. Goldstein, *Free Radic. Biol. Med.*, **44**, 2013 (2008); https://doi.org/10.1016/j.freeradbiomed.2008.02.015
70. M. Valko, D. Leibfritz, J. Moncol, M.T.D. Cronin, M. Mazur and J. Telser, *Int. J. Biochem. Cell Biol.*, **39**, 44 (2007); https://doi.org/10.1016/j.biocel.2006.07.001
71. F. Ursini, M. Maiorino and H.J. Forman, *Redox Biol.*, **8**, 205 (2016); https://doi.org/10.1016/j.redox.2016.01.010
72. L.A. Pham-Huy, H. He and C. Pham-Huy, *Int. J. Biomed. Sci.*, **4**, 89 (2008).
73. S. Noori, *J. Clin. Cell. Immunol.*, **1**, 413 (2012); https://doi.org/10.4172/scientificreports.413
74. J. Bouayed and T. Bohn, Nutrition, Well-Being and Health, InTech (2012).
75. C. Kerksick and D. Willoughby, *J. Int. Soc. Sports Nutr.*, **2**, 38 (2005); https://doi.org/10.1186/1550-2783-2-2-38
76. A.C. Carr and B. Frei, *Am. J. Clin. Nutr.*, **69**, 1086 (1999); https://doi.org/10.1093/ajcn/69.6.1086
77. H. Sies, Oxidative Stress, In: Oxidants and Antioxidants, Academic Press, New York (1991).
78. E.W. Neuman, *J. Chem. Phys.*, **2**, 31 (1934); https://doi.org/10.1063/1.1749353
79. A.W. Petrocelli and D.L. Kraus, *J. Chem. Educ.*, **40**, 146 (1963); https://doi.org/10.1021/ed040p146
80. C.B. Jackson and R.C. Werner, *Adv. Chem. Ser.*, **19**, 169 (1957); https://doi.org/10.1021/ba-1957-0019.ch018
81. M. Schmidt and H. Bipp, *Z. Anorg. Allg. Chem.*, **303**, 190 (1960); https://doi.org/10.1002/zaac.19603030312
82. A. Le Berre and Y. C. R. Berber, *Acad. Sci. Paris,* **260**, 4299 (1965).
83. A. Le Berre and Y. Berguer, *Bull. Soc. Chim. Fr.*, **85**, 2363 (1966).
84. B.H.J. Bielski and J.M. Gebicki, *Adv. Radiat. Chem.*, **2**, 177 (1970).
85. G. Czapski, *Annu. Rev. Phys. Chem.*, **22**, 171 (1971); https://doi.org/10.1146/annurev.pc.22.100171.001131
86. P.F. Knowles, J.F. Gibson, F.M. Pick and R.C. Bray, *Biochem. J.*, **111**, 53 (1969); https://doi.org/10.1042/bj1110053
87. J.M. McCord and I. Fridovich, *J. Biol. Chem.*, **244**, 6049 (1969); https://doi.org/10.1016/S0021-9258(18)63504-5
88. J.S. Valentine and D. Mota de Freitas, *J. Chem. Educ.*, **62**, 990 (1985); https://doi.org/10.1021/ed062p990
89. C.S. St. Clair, H.B. Gray and J.S. Valentine, *Inorg. Chem.*, **31**, 925 (1992); https://doi.org/10.1021/ic00031a041
90. J.A. Fee, Eds.: M.A.J. Rodgers and E.L. Powers, Oxygen and Oxy-Radicals in Chemistry and Biology, Academic Press: New York (1981).
91. I. Fridovich, *Adv. Inorg. Biochem.*, **1**, 67 (1979).
92. A. Bakac, J.H. Espenson, I.I. Creaser and A.M. Sargeson, *J. Am. Chem. Soc.*, **105**, 7624 (1983); https://doi.org/10.1021/ja00364a025
93. W.H. Bannister and J.V. Bannister, Biological and Clinical Aspects of Superoxide and Superoxide Dismutase, Elsevier: Amsterdam (1980).
94. R. Nilsson, F.M. Pick and R.C. Bray, *Biochim. Biophys. Acta*, **145**, 145 (1969); https://doi.org/10.1016/0304-4165(69)90022-1
95. I. Fridovich, *Acc. Chem. Res.*, **5**, 321 (1972); https://doi.org/10.1021/ar50058a001
96. B.H.J. Bielski, *Photochem. Photobiol.*, **28**, 645 (1978); https://doi.org/10.1111/j.1751-1097.1978.tb06986.x
97. B.H.J. Bielski, D.E. Cabelli, R.L. Arudi and A.B. Ross, *J. Phys. Chem. Ref. Data*, **14**, 1041 (1985); https://doi.org/10.1063/1.555739
98. P.J. Wardman, *J. Phys. Chem. Ref. Data*, **18**, 1637 (1989); https://doi.org/10.1063/1.555843
99. D.M. Stanbury, *Adv. Inorg. Chem.*, **33**, 69 (1989).
100. L. Vaska, *Acc. Chem. Res.*, **9**, 175 (1976); https://doi.org/10.1021/ar50101a002
101. L. Andrews, *J. Am. Chem. Soc.*, **90**, 7368 (1968); https://doi.org/10.1021/ja01028a048
102. J.C. Evans, *J. Chem. Soc. D*, 682 (1969); https://doi.org/10.1039/c29690000682
103. T. Ozawa, A. Hanaki and H. Yamamoto, *FEBS Lett.*, **74**, 99 (1977); https://doi.org/10.1016/0014-5793(77)80762-X
104. P. Geroge, Eds,: T.E. King, H.S. Mason and M. Morrison, Oxidases and Related Redox Systems, Wiley: New York (1965).
105. J.A. Fee and J.S. Valentine, Eds.: A.M. Michelson, J.M. Mecord and I. Fridovich, Superoxide and Superoxide Dismutase, Academic Press: New York (1977).
106. M. Faraggi and C. Houee-Levin, *J. Chim. Phys.*, **96**, 71 (1999); https://doi.org/10.1051/jcp:1999113
107. D. Solomon, P. Peretz and M. Faraggi, *J. Phys. Chem.*, **86**, 1842 (1982); https://doi.org/10.1021/j100207a021
108. R. Dietz, A.E.J. Fomo, B.E. Larcombe and M.E. Peover, *J. Chem. Soc. B*, 816 (1970); https://doi.org/10.1039/J29700000816
109. F. Magno, R. Seeber and S. Valcher, *J. Electroanal. Chem.*, **83**, 131 (1977); https://doi.org/10.1016/S0022-0728(77)80506-8
110. R.A. Johnson and E.G. Nidy, *J. Org. Chem.*, **40**, 1680 (1975); https://doi.org/10.1021/jo00899a049
111. D.T. Sawyer, D.T. Richens, E.J. Nanni Jr. and M.D. Stallings, Eds.: J.V. Bannister and H.A.O. Hill, Redox Reaction Chemistry of Superoxide Ion, In: Chemical and Biochemical Aspects of Superoxide and Superoxide Dismutase: Developments in Biochemistry; Elsevier/North-Holland: New York, vol. 11A, pp 1-23 (1979).
112. E.J. Nanni Jr., Ph.D. Dissertation, University of California, Riverside, CA, USA (1980).
113. E.A. Mayeda and A.J. Bard, *J. Am. Chem. Soc.*, **95**, 6223 (1973); https://doi.org/10.1021/ja00800a012
114. R.M. Sellers and M.G. Simic, *J. Am. Chem. Soc.*, **98**, 6145 (1976); https://doi.org/10.1021/ja00436a014
115. D.T. Sawyer, M.J. Gibian, M.M. Morrison and E.T. Seo, *J. Am. Chem. Soc.*, **100**, 627 (1978); https://doi.org/10.1021/ja00470a046
116. M. Tezuka, H. Hamada, Y. Ohkatsu and T. Osa, *Denki Kagaku Oyobi Kogyo Butsuri Kagaku*, **44**, 17 (1976); https://doi.org/10.5796/kogyobutsurikagaku.44.17
117. Y.A. Ilan, G. Czapanki and D. Meisel, *Biochim. Biophys. Acta*, **430**, 209 (1976); https://doi.org/10.1016/0005-2728(76)90080-3
118. D. Behar, G. Czapski, J. Rabani, L.M. Dorfman and H.A. Schwarz, *J. Phys. Chem.*, **74**, 3209 (1970); https://doi.org/10.1021/j100711a009
119. G.W. Gokel, H.M. Gerdes and N.W. Rebert, *Tetrahedron Lett.*, **17**, 653 (1976); https://doi.org/10.1016/S0040-4039(00)74588-6
120. J.A. Imlay and S. Linn, *Science*, **240**, 1302 (1988); https://doi.org/10.1126/science.3287616
121. E.R. Stadtman, *Science*, **257**, 1220 (1992); https://doi.org/10.1126/science.1355616
122. C.E. Thomas, L.A. Morehouse and S.D. Aust, *J. Biol. Chem.*, **260**, 3275 (1985); https://doi.org/10.1016/S0021-9258(19)83617-7

123. B.M. Babior, R.S. Kipnes and J.T. Curnutte, *J. Clin. Invest.*, **52**, 741 (1973); https://doi.org/10.1172/JCI107236
124. J.T. Curnutte and B.M. Babior, *J. Clin. Invest.*, **53**, 1662 (1974); https://doi.org/10.1172/JCI107717
125. B.M. Babior, *Braz. J. Med. Biol. Res.*, **30**, 141 (1997); https://doi.org/10.1590/S0100-879X1997000200001
126. R.B. Johnston Jr. and S.L. Newman, *Pediatr. Clin. North Am.*, **24**, 365 (1977); https://doi.org/10.1016/S0031-3955(16)33424-1
127. S.J. Chanock, J. El Benna, R.M. Smith and B.M. Babior, *J. Biol. Chem.*, **269**, 24519 (1994); https://doi.org/10.1016/S0021-9258(17)31418-7
128. C.C. Winterbourn, *Arch. Biochem. Biophys.*, **209**, 159 (1981); https://doi.org/10.1016/0003-9861(81)90268-X
129. E. Cadenas, *Annu. Rev. Biochem.*, **58**, 79 (1989); https://doi.org/10.1146/annurev.bi.58.070189.000455
130. D.R. Gough and T.G. Cotter, Cell Death and Disease, Macmillan Publishers Limited (2011).
131. R.J. Campion, N. Purdie and N. Sutin, *Inorg. Chem.*, **3**, 1091 (1964); https://doi.org/10.1021/ic50018a006
132. T.J. Meyer and H. Taube, *Inorg. Chem.*, **7**, 2369 (1968); https://doi.org/10.1021/ic50069a038
133. M. Chou, C. Creutz and N. Sutin, *J. Am. Chem. Soc.*, **99**, 5615 (1977); https://doi.org/10.1021/ja00459a014
134. W. Böttcher, G.M. Brown and N. Sutin, *Inorg. Chem.*, **18**, 1447 (1979); https://doi.org/10.1021/ic50196a008
135. J.C. Brodovitch and A. McAuley, *Inorg. Chem.*, **20**, 1667 (1981); https://doi.org/10.1021/ic50220a009
136. B. Goyal, S. Solanki, S. Arora, A. Prakash and R.N. Mehrotra, *J. Chem. Soc., Dalton Trans.*, 3109 (1995); https://doi.org/10.1039/dt9950003109
137. M. Martinez and M.A. Pitarque, *J. Chem. Soc., Dalton Trans.*, 4107 (1995); https://doi.org/10.1039/dt9950004107
138. D. Chatterjee, *J. Chem. Soc., Dalton Trans.*, 4389 (1996); https://doi.org/10.1039/DT9960004389
139. T.C. Lau, K.W.C. Lau and K. Lau, *J. Chem. Soc., Dalton Trans.*, 3091 (1994); https://doi.org/10.1039/dt9940003091
140. M. Martinez, M.A. Pitarque and R. van Eldik, *J. Chem. Soc., Dalton Trans.*, 3159 (1994); https://doi.org/10.1039/dt9940003159
141. D.H. Macartney and A. McAuley, *Inorg. Chem.*, **22**, 2062 (1983); https://doi.org/10.1021/ic00156a024
142. K. Lemma, A.M. Sargeson and L.I. Elding, *J. Chem. Soc., Dalton Trans.*, 1167 (2000); https://doi.org/10.1039/a909484i
143. R.A. Marcus and N. Sutin, *Biochim. Biophys. Acta Rev. Bioenerg.*, **811**, 265 (1985); https://doi.org/10.1016/0304-4173(85)90014-X
144. L. Pauling and E.B. Wilson, Introduction to Quantum Mechanics, McGraw Hill: New York (1935).
145. M.A. Ratner and R.D. Levine, *J. Am. Chem. Soc.*, **102**, 4898 (1980); https://doi.org/10.1021/ja00535a010
146. M.H. Ford-Smith and N. Sutin, *J. Am. Chem. Soc.*, **83**, 1830 (1961); https://doi.org/10.1021/ja01469a015
147. G. Dulz and N. Sutin, *Inorg. Chem.*, **2**, 917 (1963); https://doi.org/10.1021/ic50009a010
148. M. Smoluchowski, *Z. Phys. Chem.*, **92U**, 129 (1918); https://doi.org/10.1515/zpch-1918-9209
149. R.A. Marcus, *Rev. Mod. Phys.*, **65**, 599 (1993); https://doi.org/10.1103/RevModPhys.65.599
150. R.A. Marcus, *Angew. Chem. Int. Ed. Engl.*, **32**, 1111 (1993); https://doi.org/10.1002/anie.199311113
151. A. Bakac, Physical Inorganic Chemistry: Reactions, Processes and Applications, John Wiley & Sons, Inc.: Hoboken, New Jersey (2010).
152. S. Wherland, *Coord. Chem. Rev.*, **123**, 169 (1993); https://doi.org/10.1016/0010-8545(93)85055-9
153. T.W. Swaddle, *Chem. Rev.*, **105**, 2573 (2005); https://doi.org/10.1021/cr030727g
154. R.A. Marcus, *J. Phys. Chem. B*, **102**, 10071 (1998); https://doi.org/10.1021/jp9834457
155. J.M. Savéant, *J. Am. Chem. Soc.*, **130**, 4732 (2008); https://doi.org/10.1021/ja077480f
156. D.M. Stanbury, O. Haas and H. Taube, *Inorg. Chem.*, **19**, 518 (1980); https://doi.org/10.1021/ic50204a048
157. K. Zahir, J.H. Espenson and A. Bakac, *J. Am. Chem. Soc.*, **110**, 5059 (1988); https://doi.org/10.1021/ja00223a025
158. R.B. Jordan, Reaction Mechanisms of Inorganic and Organometallic Systems, Oxford University Press: New York (1991).
159. N. Sutin, *Acc. Chem. Res.*, **15**, 275 (1982); https://doi.org/10.1021/ar00081a002
160. N. Sutin, *Prog. Inorg. Chem.*, **30**, 441 (1983).
161. J.J. Zuckerman, Inorganic Reactions and Methods, VCH Publishers, Weinheim, Decrfield Beach, FL, vol. 15 (1986).
162. N.S. Hush, *Trans. Faraday Soc.*, **57**, 557 (1961); https://doi.org/10.1039/tf9615700557
163. N.R. Kestner, J. Logan and J. Jortner, *J. Phys. Chem.*, **78**, 2148 (1974); https://doi.org/10.1021/j100614a017
164. C.T. Lin, W. Boettcher, M. Chou, C. Creutz and N. Sutin, *J. Am. Chem. Soc.*, **98**, 6536 (1976); https://doi.org/10.1021/ja00437a020
165. J. Ulstrap, Charge Transfer Processes in Condensed Media, Springer: Verlag, Berlin (1979).
166. D. Newton and N. Sutin, *Annu. Rev. Phys. Chem.*, **35**, 437 (1984); https://doi.org/10.1146/annurev.pc.35.100184.002253
167. L.E. Bennett and H. Taube, *Inorg. Chem.*, **7**, 254 (1968); https://doi.org/10.1021/ic50060a017
168. J.R. Pladziewicz and J.H. Espenson, *J. Phys. Chem.*, **75**, 3381 (1971); https://doi.org/10.1021/j100690a034
169. Y. Tendler and M. Faraggi, *J. Chem. Phys.*, **57**, 1358 (1972); https://doi.org/10.1063/1.1678404
170. R.J. Christensen, J.H. Espenson and A.B. Butcher, *Inorg. Chem.*, **12**, 564 (1973); https://doi.org/10.1021/ic50121a014
171. H.E. Toma and J.M. Malin, *J. Am. Chem. Soc.*, **97**, 288 (1975); https://doi.org/10.1021/ja00835a010
172. D.E. Pennington and A.E. Martell, Coordination Chemistry, ed. ACS Monograph 174, ACS: Washington D.C., vol. 2 (1978).
173. C.A. Koval and D.W. Margerum, *Inorg. Chem.*, **20**, 2311 (1981); https://doi.org/10.1021/ic50221a074
174. D.H. Macartney and N. Sutin, *Inorg. Chem.*, **24**, 3403 (1985); https://doi.org/10.1021/ic00215a022
175. J.W. Herbert and D.H. Macartney, *Inorg. Chem.*, **24**, 4398 (1985); https://doi.org/10.1021/ic00219a040
176. M.N. Doyle, K. Libson, M. Woods, J.C. Sullivan and E. Deutsch, *Inorg. Chem.*, **25**, 3367 (1986); https://doi.org/10.1021/ic00239a011
177. J.R. Pladziewicz, A.J. Abrahamson, R.A. Davis and M.D. Likar, *Inorg. Chem.*, **26**, 2058 (1987); https://doi.org/10.1021/ic00260a010
178. H. Doine and T.W. Swaddle, *Inorg. Chem.*, **27**, 665 (1988); https://doi.org/10.1021/ic00277a019
179. K. Libson, M. Woods, J.C. Sullivan, J.W. Watkins II, R.C. Elder and E. Deutsch, *Inorg. Chem.*, **27**, 999 (1988); https://doi.org/10.1021/ic00279a013
180. J.M.A. Hoddenbagh and D.H. Macartney, *Inorg. Chem.*, **29**, 245 (1990); https://doi.org/10.1021/ic00327a019
181. M.S. Ram and A. Haim, *Inorg. Chem.*, **30**, 1319 (1991); https://doi.org/10.1021/ic00006a029
182. R. Sarala, S.B. Rabin and D.M. Stanbury, *Inorg. Chem.*, **30**, 3999 (1991); https://doi.org/10.1021/ic00021a007
183. S.A. Kazmi, A.L. Shorter and J.V. McArdle, *Inorg. Chem.*, **23**, 4332 (1984); https://doi.org/10.1021/ic00193a045
184. T.W. Newton, *J. Chem. Educ.*, **45**, 571 (1968); https://doi.org/10.1021/ed045p571
185. W.L. Reynolds and R.W. Lumry, Mechanisms of Electron Transfer, Ronald Press: New York (1966).
186. P.W. Atkins and M.C.R. Symons, The Structure of Inorganic Radicals, Elsevier: New York (1967).
187. A.F. Wells, Structural Inorganic Chemistry, Clarendon Press: Oxford, Edn. 4 (1975).
188. M.C.R. Symons, *J. Chem. Soc., Dalton Trans.*, 1468 (1979); https://doi.org/10.1039/dt9790001468
189. W.K. Wilmarth, D.M. Stanbury, J.E. Byrd, H.N. Po and C. Chua, *Coord. Chem. Rev.*, **51**, 155 (1983); https://doi.org/10.1016/0010-8545(83)85010-3
190. R. Sarala, M.S. Islam, S.B. Rabin and D.M. Stanbury, *Inorg. Chem.*, **29**, 1133 (1990); https://doi.org/10.1021/ic00331a006

191. R.B. Jordon, Reaction Mechanism of Inorgani and Organometallic Systems, Oxford University Press (1991).
192. D.L. Ball and E.L. King, *J. Am. Chem. Soc.*, **80**, 1091 (1958); https://doi.org/10.1021/ja01538a019
193. H. Taube, H. Myers and R.L. Rich, *J. Am. Chem. Soc.*, **75**, 4118 (1953); https://doi.org/10.1021/ja01112a546
194. H. Taube, *Adv. Inorg. Chem.*, **1**, 1 (1959); https://doi.org/10.1016/S0065-2792(08)60251-4
195. P. George, J.S. Griffith. P.D. Boyer, H. Lardy and K. Myrbäck, The Enzymes, Academic Press, New York, vol. 1, p. 347 (1959).
196. R.G. Wilkins, Kinetics and Mechanism of Reactions of Transition Metal Complexes, Weinheim: New York (1991).
197. F.A. Cotton and G. Wilkinson, Advance Inorganic Chemistry, A Comprehensive Text, Wiley Eastern Limited,:New Delhi, Edn. 3 (1990).
198. A. Adin and A.G. Sykes, *J. Chem. Soc. A*, 354 (1968); https://doi.org/10.1039/J19680000354
199. A. Haim and N. Sutin, *J. Am. Chem. Soc.*, **87**, 4210 (1965); https://doi.org/10.1021/ja01096a051
200. J. Halpern and S. Nakamura, *J. Am. Chem. Soc.*, **87**, 3002 (1965); https://doi.org/10.1021/ja01091a036
201. R. Snellgrove and E.L. King, *J. Am. Chem. Soc.*, **84**, 4609 (1962); https://doi.org/10.1021/ja00882a060
202. R. Snellgrove and E.L. King, *Inorg. Chem.*, **3**, 288 (1964); https://doi.org/10.1021/ic50012a038
203. D.P. Fay and N. Sutin, *Inorg. Chem.*, **9**, 1291 (1970); https://doi.org/10.1021/ic50087a064
204. K. Wieghardt and A.G. Sykes, *J. Chem. Soc., Dalton Trans.*, 651 (1974); https://doi.org/10.1039/DT9740000651
205. J. Halpern and L.E. Orgel, *Discuss. Faraday Soc.*, **29**, 7 (1960); https://doi.org/10.1039/DF9602900007
206. H. Taube and R.G. Gaunder, *Inorg. Chem.*, **9**, 2627 (1970); https://doi.org/10.1021/ic50094a001
207. F.R. Nordmeyer and C. Norris, *J. Am. Chem. Soc.*, **93**, 4044 (1971); https://doi.org/10.1021/ja00745a037
208. E.S. Gould and J.R. Barber Jr, *J. Am. Chem. Soc.*, **93**, 4045 (1971); https://doi.org/10.1021/ja00745a038
209. E.S. Gould, *J. Am. Chem. Soc.*, **94**, 4360 (1972); https://doi.org/10.1021/ja00767a064
210. M.Z. Hoffman and M. Simic, *J. Am. Chem. Soc.*, **94**, 1757 (1972); https://doi.org/10.1021/ja00760a063
211. A. Haim, *Acc. Chem. Res.*, **8**, 264 (1975); https://doi.org/10.1021/ar50092a002
212. E.S. Gould, *J. Am. Chem. Soc.*, **96**, 2373 (1974); https://doi.org/10.1021/ja00815a011
213. R.J. Campion, T.J. Conocchioli and N. Sutin, *J. Am. Chem. Soc.*, **86**, 4591 (1964); https://doi.org/10.1021/ja01075a015
214. R.G. Linck, Eds.: M.L. Tobe, MTP International Review of Science, Inorganic Chemistry, Series one, Butterworth: London (1972).
215. W.S. Melvin and A. Haim, *Inorg. Chem.*, **16**, 2016 (1977); https://doi.org/10.1021/ic50174a038
216. R.A. Marusak, P. Osvath, M. Kemper and A.G. Lappin, *Inorg. Chem.*, **28**, 1542 (1989); https://doi.org/10.1021/ic00307a024
217. R.C. Patel, R.E. Ball, J.F. Endicott and R.G. Hughes, *Inorg. Chem.*, **9**, 23 (1970); https://doi.org/10.1021/ic50083a005
218. U. El-Ayaan, R. F. Jameson and W. Linert, *J. Chem. Soc., Dalton Trans.*, 1315 (1998); https://doi.org/10.1039/a708639c
219. M. Ardon and R.A. Plane, *J. Am. Chem. Soc.*, **81**, 3197 (1959); https://doi.org/10.1021/ja01522a008
220. J. Halpern, *Q. Rev. Chem. Soc.*, **15**, 207 (1961); https://doi.org/10.1039/qr9611500207
221. J.H. Espenson, *Acc. Chem. Res.*, **3**, 347 (1970); https://doi.org/10.1021/ar50034a004
222. J.K. Beattie and G.P. Haight Jr., *Prog. Inorg. Chem.*, **17**, 93 (1972).
223. R.G. Linck, Eds.: M.L. Tobe, MTP International Review of Science, Inorganic Chemistry, Series two, Butterworth: London, vol. 9, p. 173 (1974).
224. F. Basolo and R.G. Pearson, Mechanisms of Inorganic Reactions, Wiley Eastern Limited: New Delhi, Edn. 2, Chap. 6 (1977).
225. H. Taube and E.L. King, *J. Am. Chem. Soc.*, **76**, 4053 (1954); https://doi.org/10.1021/ja01644a077
226. H.A. Schwarz, D. Comstock, J.K. Yandell and R.W. Dodson, *J. Phys. Chem.*, **78**, 488 (1974); https://doi.org/10.1021/j100598a005
227. R.G. Linck, Eds.: I.M. Kolthoff and P.J. Elving, Treatise on Analytical Chemistry, Part 1, Wiley: New York (1979).
228. F.L. Harris and D.L. Toppen, *Inorg. Chem.*, **17**, 74 (1978); https://doi.org/10.1021/ic50179a016
229. J.M. Mayer and I.J. Rhile, *Biochim. Biophys. Acta*, **1655**, 51 (2004); https://doi.org/10.1016/j.bbabio.2003.07.002
230. K. Chen, J. Hirst, R. Camba, C.A. Bonagura, C.D. Stout, B.K. Burgess and F.A. Armstrong, *Nature*, **405**, 814 (2000); https://doi.org/10.1038/35015610
231. M.V. Huynh and T.J. Meyer, *Chem. Rev.*, **107**, 5004 (2007); https://doi.org/10.1021/cr0500030
232. J. Hudis and R.W. Dodson, *J. Am. Chem. Soc.*, **78**, 911 (1956); https://doi.org/10.1021/ja01586a011
233. N. Grover and H.H. Thorp, *J. Am. Chem. Soc.*, **113**, 7030 (1991); https://doi.org/10.1021/ja00018a048
234. W. Lui and H.H. Thorp, *Transition Met. Coord. Chem.*, **1**, 187 (1996).
235. R.I. Cukier, *J. Phys. Chem.*, **98**, 2377 (1994); https://doi.org/10.1021/j100060a027
236. J.Y. Fang and S. Hammes-Schiffer, *J. Chem. Phys.*, **106**, 8442 (1997); https://doi.org/10.1063/1.473903
237. R.I. Cukier and D.G. Nocera, *Annu. Rev. Phys. Chem.*, **49**, 337 (1998); https://doi.org/10.1146/annurev.physchem.49.1.337
238. C.W. Hoganson and G.T. Babcock, *Science*, **277**, 1953 (1997); https://doi.org/10.1126/science.277.5334.1953
239. C. Costentin, D.H. Evans, M. Robert, J.-M. Savéant and P.S. Singh, *J. Am. Chem. Soc.*, **127**, 12490 (2005); https://doi.org/10.1021/ja053911n
240. S. Hammes-Schiffer, *Acc. Chem. Res.*, **34**, 273 (2001); https://doi.org/10.1021/ar9901117
241. J.M. Mayer, *Annu. Rev. Phys. Chem.*, **55**, 363 (2004); https://doi.org/10.1146/annurev.physchem.55.091602.094446
242. F. Himo and P.E.M. Siegbahn, *Chem. Rev.*, **103**, 2421 (2003); https://doi.org/10.1021/cr020436s
243. J.S. Wright, E.R. Johnson and G.A. Di Labio, *J. Am. Chem. Soc.*, **123**, 1173 (2001); https://doi.org/10.1021/ja002455u
244. M. Leopoldini, T. Marino, N. Russo and M. Toscano, *J. Phys. Chem. A*, **108**, 4916 (2004); https://doi.org/10.1021/jp037247d
245. P. Alov, I. Tsakovska and I. Pajeva, *Curr. Top. Med. Chem.*, **15**, 85 (2015); https://doi.org/10.2174/1568026615666141209143702
246. G. Litwinienko and K.U. Ingold, *Acc. Chem. Res.*, **40**, 222 (2007); https://doi.org/10.1021/ar0682029
247. R.D. Cannon, Electron Transfer Reactions, Butterworths (1980).
248. B. Ahrens, M.G. Davidson, V.T. Forsyth, M.F. Mahon, A.L. Johnson, S.A. Mason, R.D. Price and P.R. Raithby, *J. Am. Chem. Soc.*, **123**, 9164 (2001); https://doi.org/10.1021/ja015849+
249. G. Litwinienko and K.U. Ingold, *J. Org. Chem.*, **69**, 5888 (2004); https://doi.org/10.1021/jo049254j
250. J. Stubbe and W. van der Donk, *Chem. Rev.*, **98**, 705 (1998); https://doi.org/10.1021/cr9400875
251. C. Aubert, M.H. Vos, P. Mathis, A.P.M. Eker and K. Brettel, *Nature*, **405**, 586 (2000); https://doi.org/10.1038/35014644
252. G.T. Babcock, *Proc. Natl. Acad. Sci. USA*, **96**, 12971 (1999); https://doi.org/10.1073/pnas.96.23.12971
253. J. Stubbe, D.G. Nocera, C.S. Yee and M.C.Y. Chang, *Chem. Rev.*, **103**, 2167 (2003); https://doi.org/10.1021/cr020421u
254. G.L. Closs and J.R. Miller, *Science*, **240**, 440 (1988); https://doi.org/10.1126/science.240.4851.440
255. A. Magnuson, H. Berglund, P. Korall, L. Hammarström, B. Åkermark, S. Styring and L. Sun, *J. Am. Chem. Soc.*, **119**, 10720 (1997); https://doi.org/10.1021/ja972161h
256. M. Sjödin, S. Styring, B. Åkermark, L. Sun and L. Hammarström, *J. Am. Chem. Soc.*, **122**, 3932 (2000); https://doi.org/10.1021/ja993044k
257. A. Masarwa and D. Meyerstein, *Adv. Inorg. Chem.*, **55**, 271 (2004).
258. K.L. Rollick and J.K. Kochi, *J. Am. Chem. Soc.*, **104**, 1319 (1982); https://doi.org/10.1021/ja00369a030

259. R.A. Marcus, *J. Chem. Phys.*, **24**, 966 (1956); https://doi.org/10.1063/1.1742723
260. N. Sutin, *J. Phys. Chem.*, **90**, 3465 (1986); https://doi.org/10.1021/j100407a002
261. W. Fujita and K. Awaga, *J. Am. Chem. Soc.*, **123**, 3601 (2001); https://doi.org/10.1021/ja002873z
262. C.G. Pierpont and C.W. Lange, *Prog. Inorg. Chem.*, **41**, 331 (1994).
263. J.M. Manriquez, G.T. Yee, R.S. McLean, A.J. Epstein and J.S. Miller, *Science*, **252**, 1415 (1991); https://doi.org/10.1126/science.252.5011.1415
264. H. Zhao Jr., M.J. Bazile Jr., J.R. Gal'an-Mascaros and K.R. Dunbar, *Angew. Chem. Int. Ed.*, **42**, 1015 (2003); https://doi.org/10.1002/anie.200390259
265. J.B. Gilroy, S.D.J. McKinnon, B.D. Koivisto and R.G. Hicks, *Org. Lett.*, **9**, 4837 (2007); https://doi.org/10.1021/ol702163a
266. W. Lu, Y. Zhang, J. Dai, Q.Y. Zhu, G.Q. Bian and D.Q. Zhang, *Eur. J. Inorg. Chem.*, **2006**, 1629 (2006); https://doi.org/10.1002/ejic.200500945
267. M. Gandelman, B. Rybtchinski, N. Ashkenazi, R.M. Gauvin and D. Milstein, *J. Am. Chem. Soc.*, **123**, 5372 (2001); https://doi.org/10.1021/ja0157393
268. A.E.J. deNooy, A.C. Besemer and H. vanBekkum, *Synthesis*, 1153 (1996); https://doi.org/10.1055/s-1996-4369
269. R.A. Sheldon and I. Arends, *J. Mol. Catal. Chem.*, **251**, 200 (2006); https://doi.org/10.1016/j.molcata.2006.02.016
270. P. Chaudhuri and K. Wieghardt, *Prog. Inorg. Chem.*, **50**, 151 (2001).
271. C.K. Jørgensen, Oxidation Numbers and Oxidation States, Spinger: Berlin (1969).
272. B. de Bruin, D.G.H. Hetterscheid, A.J.J. Koekoek and H. Grützmacher, *Prog. Inorg. Chem.*, **55**, 247 (2007).
273. N.G. Connelly, R.L. Kelly, M.D. Kitchen, R.M. Mills, R.F.D. Stansfield, M.W. Whiteley, S.M. Whiting and P. Woodward, *J. Chem. Soc*., *Dalton Trans.*, 1317 (1981); https://doi.org/10.1039/DT9810001317
274. N.G. Connelly, P.G. Graham and J.B. Sheridan, *J. Chem. Soc*., *Dalton Trans.*, 1619 (1986); https://doi.org/10.1039/DT9860001619
275. R.P. Aggarwal, N.G. Connelly, B.J. Dunne, M. Gilbert and A.G. Orpen, *J. Chem. Soc., Dalton Trans.*, 1 (1991); https://doi.org/10.1039/DT9910000001
276. L. Brammer, N.G. Connelly, J. Edwin, W.E. Geiger, A.G. Orpen and J.B. Sheridan, *Organometallics*, **7**, 1259 (1988); https://doi.org/10.1021/om00096a004
277. T.F. Block, R.F. Fenske and C.P. Casey, *J. Am. Chem. Soc.*, **98**, 441 (1976); https://doi.org/10.1021/ja00418a019
278. P.J. Krusic, U. Klabunde, C.P. Casey and T.F. Block, *J. Am. Chem. Soc.*, **98**, 2015 (1976); https://doi.org/10.1021/ja00423a086
279. B. Meunier, S.P. de Visser and S. Shaik, *Chem. Rev.*, **104**, 3947 (2004); https://doi.org/10.1021/cr020443g
280. R. Liu, K. Morokuma, A.M. Mebel and M.C. Lin, *J. Phys. Chem.*, **100**, 9314 (1996); https://doi.org/10.1021/jp953566w
281. K. Rachlewicz and L. Latos-Grazynski, *Inorg. Chem.*, **35**, 1136 (1996); https://doi.org/10.1021/ic950876k
282. M.W. Renner and J. Fajer, *J. Biol. Inorg. Chem.*, **6**, 823 (2001); https://doi.org/10.1007/s007750100276
283. J.I. van der Vlugt, *Eur. J. Inorg. Chem.*, **2012**, 363 (2012); https://doi.org/10.1002/ejic.201100752
284. V. Lyaskovskyy and B. de Bruin, *ACS Catal.*, **2**, 270 (2012); https://doi.org/10.1021/cs200660v
285. W. Kaim and B. Schwederski, *Coord. Chem. Rev.*, **254**, 1580 (2010); https://doi.org/10.1016/j.ccr.2010.01.009
286. M.A. Bigi, S.A. Reed and M.C. White, *Nat. Chem.*, **3**, 216 (2011); https://doi.org/10.1038/nchem.967
287. A. Caneschi, D. Gatteschi, R. Sessoli and P. Rey, *Acc. Chem. Res.*, **22**, 392 (1989); https://doi.org/10.1021/ar00167a004
288. H. Zimmer, D.C. Lankin and S.W. Horgan, *Chem. Rev.*, **71**, 229 (1971); https://doi.org/10.1021/cr60270a005
289. F.A. Chavez and P.K. Mascharak, *Acc. Chem. Res.*, **33**, 539 (2000); https://doi.org/10.1021/ar990089h
290. L.I. Simandi, Catalytic Activation of Dioxygen by Metal Complexes, Kluwer Academic Publishers (1992).
291. A. Samuni and G. Czapski, *J. Phys. Chem.*, **74**, 4592 (1970); https://doi.org/10.1021/j100720a024
292. H. Mimoun, L. Saussine, E. Daire, M. Postel, J. Fischer and R. Weiss, *J. Am. Chem. Soc.*, **105**, 3101 (1983); https://doi.org/10.1021/ja00348a025
293. B. Meunier, Biomimetic Oxidations Catalyzed by Transition Metal Complexes, Imperial College Press: London (2000).
294. A.E. Shilov and G.B. Shulpin, Activation and Catalytic Reactions of Saturated Hydrocarbons in the Presence of Metal Complexes, Kluwer (2000).
295. I.B. Afanasiev, *Usp. Khim.*, **48**, 977 (1979).
296. A. Bakac, *Coord. Chem. Rev.*, **250**, 2046 (2006); https://doi.org/10.1016/j.ccr.2006.02.001
297. M.F. Perutz, *Nature*, **228**, 726 (1970); https://doi.org/10.1038/228726a0
298. C.G. Barraclough, G.A. Lawrance and P.A. Lay, *Inorg. Chem.*, **17**, 3317 (1978); https://doi.org/10.1021/ic50190a001
299. T. Shibahara, *J. Chem. Soc. Chem. Commun.*, 864 (1973); https://doi.org/10.1039/C39730000864
300. A. Hoffman and H. Taube, *Inorg. Chem.*, **7**, 1971 (1968); https://doi.org/10.1021/ic50068a003
301. K.M. Davies and A.G. Sykes, *J. Chem. Soc. A*, 1418 (1971); https://doi.org/10.1039/j19710001418
302. M.R. Hyde and A.G. Sykes, *J. Chem. Soc., Dalton Trans.*, 1550 (1974); https://doi.org/10.1039/DT9740001550
303. R. Davies and A.G. Sykes, *J. Chem. Soc. A*, 2831 (1968); https://doi.org/10.1039/j19680002831
304. Y. Sasaki, *Bull. Chem. Soc. Jpn.*, **50**, 1939 (1977); https://doi.org/10.1246/bcsj.50.1939
305. E.P. Talsi, V.P. Babenko, V.M. Nekipelov and A.A. Shubin, *React. Kinet. Catal. Lett.*, **31**, 209 (1986); https://doi.org/10.1007/BF02062534
306. S.K. Ghosh, S.K. Saha, M.C. Ghosh, R.N. Bose, J.W. Reed and E.S. Gould, *Inorg. Chem.*, **31**, 3358 (1992); https://doi.org/10.1021/ic00042a007
307. D.L. Duffy, D.A. House and J.A. Weil, *J. Inorg. Nucl. Chem.*, **31**, 2053 (1969); https://doi.org/10.1016/0022-1902(69)90020-7
308. R.E. Marsh and W.P. Schaefer, *Acta Crystallogr. B*, **24**, 246 (1968); https://doi.org/10.1107/S0567740868002037
309. A.A. Vlèek, *Collect. Czech. Chem. Commun.*, **25**, 3036 (1960); https://doi.org/10.1135/cccc19603036
310. W.P. Schaefer, *Inorg. Chem.*, **7**, 725 (1968); https://doi.org/10.1021/ic50062a022
311. L. Pauling, The Nature of the Chemical Bond, Cornell University Press: New York (1960).
312. G.G. Christoph, R.E. Marsh and W.P. Schaefer, *Inorg. Chem.*, **8**, 291 (1969); https://doi.org/10.1021/ic50072a022
313. J.A. Weil and J.K. Kinnaird, *J. Phys. Chem.*, **71**, 3341 (1967); https://doi.org/10.1021/j100869a036
314. V.I. Belova and Y.R. Syrkin, *Neorg. Khim. Akad. Nauk SSSR*, **30**, 109 (1955).
315. I. Bernal, E.A.V. Ebsworth and J.A. Weil, *Proc. Chem. Soc.*, 57 (1959).
316. B.M. Hoffman, D.L. Diemente and F. Basolo, *J. Am. Chem. Soc.*, **92**, 61 (1970); https://doi.org/10.1021/ja00704a010
317. S. Barnartt and R.G. Charles, *J. Electrochem. Soc.*, **109**, 333 (1962); https://doi.org/10.1149/1.2425411
318. J.E. Barnes, J.B. Barrett, R.W. Brett and J. Brown, *J. Inorg. Nucl. Chem.*, **30**, 2207 (1968); https://doi.org/10.1016/0022-1902(68)80218-0
319. A. Haim and W.K. Wilmarth, *J. Am. Chem. Soc.*, **83**, 509 (1961); https://doi.org/10.1021/ja01464a001.
320. A.A. Gabovich and I.M. Reibel, *Tr. Kishinevsk. Sel'khoz. Inst.*, **9**, 185 (1956).
321. A.A. Gabovich and I.M. Reibel, *Tr. Kishinevsk. Sel'khoz. Inst.*, **43**, 61 (1966).
322. L.R. Thompson and W.K. Wilmarth, *J. Phys. Chem.*, **56**, 5 (1952); https://doi.org/10.1021/j150493a002
323. A.G. Sykes, *Trans. Faraday Soc.*, **59**, 1334 (1963); https://doi.org/10.1039/TF9635901334
324. K. Glau and K. Rehm, *Z. Anorg. Allg. Chem.*, **237**, 79 (1938); https://doi.org/10.1002/zaac.19382370107
325. A.G. Sykes and J.A. Weil, *Prog. Inorg. Chem.*, **1**, 13 (1970).