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General energetic criteria for the implementation of electrochemical, chemical and biochemical electron transfer processes

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This article aims at summarizing the criteria based on energetic data and kinetic rules of general validity which can be utilized to predict the feasibility of a given chemical redox process, particularly by enzymatic catalysis, and to determine the physico-chemical conditions related to the state of the solution where reagents are present which could restrain this feasibility.

When applying these criteria to the whole field of carbon chemistry in aqueous solutions, at room temperature and in the medium pH range, one is led to the conclusion that the feasible redox processes are actually much less diverse than is currently assumed without serious examination. As a matter of fact, the chemistry of life is more or less identifiable in this respect with the whole range of remaining physicochemical possibilities, without any need for qualitative supplementary restrictions, leading, e.g., to some sort of discrimination made by enzymatic sequences randomly settled by evolution. Enzyme catalysts, which are often considered to be the qualitatively determining factors of the choice of metabolic processes, are in fact only executive agents, more or less discriminative, for the whole set of processes that remain feasible when the energetic and kinetic redox reactivity of concerned substrates is correctly analyzed.

1. *Stoichiometry of redox reactions*

Oxido-reduction, or redox reactions, are usually defined as chemical transformations which can be globally described by stoichiometrically summing up the following:

a) the capture of one or several electrons by a reagent called the oxidant of the electron-accepting redox couple (1)

$$a_1\,Ox_1 + n_1\,e^- + p_1\,H^+ \rightleftharpoons b_1\,Red_1 + q_1\,H_2O;$$

b) the supply of one or several electrons by another reagent called the reductant of the donor redox couple (2):

$$a_2\,Red_2 + q_2\,H_2O \rightleftharpoons b_2\,Ox_2 + n_2\,e^- + p_2\,H^+$$

Some redox couples involve other compounds, such as NH_3 in aminating reductions of α-ketoacids or aldehydes, and HS CoA in thioesterifying oxidation of aldehydes. But such cases are better treated by complementary modifications of the theory involving additions of non-redox processes to redox couples defined as proposed above.

In fact, we will have to distinguish between the different kinds of stoichiometry of redox couples as to whether they involve

- either simply one or several electrons, as:

$$Ox + ne^- \rightleftharpoons Red$$

such as in: $Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$.

- or a proton-exchange in addition to the electron exchange as:

$$Ox + ne^- + pH^+ \rightleftharpoons Red$$

where p is always positive, such as in:

$$\text{Quinone} + 2\,e^- + 2\,H^+ \rightleftharpoons \text{Hydroquinone}$$

$$NAD^+ + 2\,e^- + H^+ \rightleftharpoons NADH.$$

- or a modification of the covalent vicinity (topology) of relatively heavy atoms (i.e. atoms other than H, such as C, O, N, S, etc.), which corresponds to the most general stoichiometry, e.g.:

$$R_1R_2R_3-COH + 2\,e^- + 2\,H^+ \rightleftharpoons R_1R_2R_3-CH + H_2O$$

$$R-CO_2^- + 2\,e^- + 3\,H^+ \rightleftharpoons R-CHO + H_2O$$

$$R-CO_2^- + CH_3\,COScoA + 2\,e^- + 3\,H^+ \rightleftharpoons R\text{–}CHOH\text{–}CH_2\text{–}COScoA + H_2O$$

$$RSSR + 2\,e^- + 2\,H^+ \rightleftharpoons 2\,RSH$$

In aqueous media, the solvated (hydrated) electron has extremely strong reducing properties ($U° = -2.7\ V/_{SHE}$) and therefore cannot exist as such at noticeable concentrations because of the formation of gaseous hydrogen by reduction of H_2O.

Consequently the balance of electrons given by Red_2 must equal the balance of electrons captured by Ox_1 and the redox reaction between both is written:

$$n_2\,a_1\,Ox_1 + n_1\,b_2\,Red_2 + (n_2\,p_1 - n_1\,p_2)\,H^+ \rightleftharpoons n_2\,b_1\,Red_1 + n_1\,a_2\,Ox_2 + (n_2\,q_1 - n_1\,q_2)\,H_2O.$$

2. *Energetic criteria for redox reactions taking place at equilibrium*

Firstly, we recall the conditions defining the direction and the equilibrium state of any given redox reaction from the initial state of an aqueous solution. These conditions are necessary, but kinetic restrictions often prevent equilibrium being reached and sometimes even prevent the reaction occurring at all. This is particularly the case for electron transfers involving 1 or 2 redox couples which imply any change of the covalent topology of their heavy atoms.

2.1. *Energetic properties of redox couples*

The chemical potential of exchangeable electrons with redox couples in solutions is currently defined in the form of the oxido-reduction (redox) potential, which represents the free enthalpy involved in the supplying of 1/F equivalent of electrons by the solution. The zero level of this redox potential is usually defined for a H^+ solution of molar activity saturated with gaseous H_2 under 1 at.

The Nernst formula, which is a mere consequence of both principles of energetics for the case of ideally diluted solutions, defines the relationship between the redox potential, U, of a solution and the nature and the concentrations of its components for any solution containing a given redox couple.

In the most general case of a redox couple obeying the stoichiometry:

$$a\,Ox + ne^- + pH^+ + r\,M \rightleftharpoons b\,Red + q\,H_2O$$

this formula can be written:

$$U = U° + \frac{RT}{nF}\ln\frac{|Ox|^a|H^+|^p|M|^r}{|Red|^b}$$

if the reference states of the dissolved components and water are respectively molar activities and unit molar fraction, i.e. pure water. If, when writing the redox couple stoichiometry, the symbol ↑ is placed behind Ox, Red or M, the components concerned are considered to be exchanged in the gaseous state, and their molarities are replaced by their partial pressures in the ln expression as well as in the definition and calculation of U° from standard free enthalpies of formation. If, similarly, the symbol ↓ appears, the components concerned are considered to be exchanged in their pure solid state and they are omitted in the ln term, but taken into account as such in the definition and calculation of U°.

$$\text{At } 25\,°C\text{:}\ \frac{2.3\,RT}{F} = 0.05916\ V.$$

In any pH region where the major protonation state of every component of a redox couple remains unchanged, the Nernst formula is usually written:

$$U = U° - \frac{2.3\,RT}{F}\,\frac{p}{n}\,(pH) + \frac{2.3\,RT}{nF}\log\frac{|Ox|^a|M|^r}{|Red|^b}$$

$$\text{with: } U°' = U° - \frac{2.3\,RT}{F}\,\frac{p}{n}\,(pH).$$

U° is the standard redox potential of the couple concerned; it corresponds to the redox potential of a solution where $|Ox| = |Red| = |M| = |H^+| = 1\,M$, i.e., at pH = 0. U°′ is currently called the apparent standard redox potential at any defined pH. It corresponds to the redox potential of a solution where $|Ox| = |Red| = |M| = 1\,M$ buffered at the concerned pH.

Diagrams for any given redox couple, U°′/pH, which represent the variations of U°′ against pH, considering all possible changes of the dominant protonation states of its components, are easily constructed[1-3] (figures 1, 3). They offer an easy way of appreciating at a glance the redox and acid-base properties of any redox couple, e.g. concerning the range of predominance of its oxidized and reduced forms in all their protonation states or its reaction capacity with any other given redox couple.

2.2. *Standard free enthalpy balance of redox reactions*

For any redox reaction, such as:

$$n_2 a_1 Ox_1 + n_1 b_2 Red_2 + (n_2 p_1 - n_1 p_2) H^+ \rightleftharpoons$$
$$n_2 b_1 Red_1 + n_1 a_2 Ox_2 (n_2 q_1 - n_1 q_2) H_2O \ldots, \Delta G^{\circ\prime}_{1/2}$$

the equilibrium condition is: $U_1 = U_2$, where U_1 and U_2 are the redox potentials of the solution calculated for the 2 redox couples Ox_1/Red_1 and Ox_2/Red_2 respectively. Consequently, the concentrations of the components of these couples will adjust from the initial state until this condition is fulfilled.

From this equality, it is easy to show that it is possible to describe the redox equilibrium at any buffered pH, by an apparent mass action law:

$$\frac{(C_{Red1})^{n2\,b1}(C_{Ox2})^{n1\,a2}}{(C_{Ox1})^{n2\,a1}(C_{Red2})^{n1\,b2}} = K'_{1/2}(pH)$$

where the symbol C represents the total concentration of the corresponding components of both couples in all their protonation states and $K'_{1/2}$ (pH) is an apparent equilibrium constant, dependent upon pH, with:

$$RT \ln K'_{1/2} = -\Delta G^{\circ\prime}_{1/2}$$

i.e., at 25 °C: $1.364\ pK'_{1/2} = \Delta G^{\circ\prime}_{1/2}$

and: $\Delta G^{\circ\prime}_{1/2} = -n_1 n_2 F (U^{\circ\prime}_1 - U^{\circ\prime}_2)$

with $n_1 n_2$ = number of electrons exchanged from $b_2 Red_2$ to $a_1 Ox_1$ and $F = 96{,}500$ coulombs $= -23.05$ kcal × V^{-1}.

Alternatively such equilibria can be more completely described if pH is not kept constant by a classical mass action law:

$$\frac{|Red_1|^{n_2 b_1}\quad |Ox_2|^{n_1 a_2}}{|Ox_1|^{n_2 a_1}|Red_2|^{n_1 b_2}|H^+|^{n_2 p_1 - n_1 p_2}} = K_{1/2}$$

with $RT \ln K_{1/2} = -\Delta G^\circ$

and $\Delta G^\circ = -n_1 n_2 F (U^\circ_1 - U^\circ_2)$.

For a most current reaction, such as:

$$Ox_1 + Red_2 + \ldots \rightleftharpoons Red_1 + Ox_2 \ldots$$

where n electrons are exchanged from Red_2 to Ox_1, when starting from equal quantities of Ox_1 and Red_2 in the absence of products, the equilibrium displacement rate is:

- about 10^{-a} if $U^{\circ\prime}_1 - U^{\circ\prime}_2 = -a\frac{0.12}{n}V$
- 0.5 if $U^{\circ\prime}_1 = U^\circ_2$
- about $(1\text{-}10^{-b})$ if $U^{\circ\prime}_1 - U^{\circ\prime}_2 = +b\frac{0.12}{n}V$.

2.3. *Associations of redox couples*

Several simple associations of redox couples are of particular importance in biochemistry.

2.3.1. Successive redox couples, dismutation reactions. When the oxidant of a first redox couple,

$$Amp + n e^- + \ldots \rightleftharpoons Red + \ldots;\ U^{\circ\prime}(A/R),$$

can be oxidized in turn as:

$$Ox + n e^- + \ldots \rightleftharpoons Amp + \ldots;\ U^{\circ\prime}(O/A),$$

it is easy to show, by considering the additivity of standard free enthalpy balances of reactions between these couples and any other reference one, that the apparent standard potential of the global couple:

$$Ox + 2 n e^- \rightleftharpoons Red + \cdots;\ U^{\circ\prime}(O/R)$$

is:

$$U^{\circ\prime}(O/R) = \frac{U^{\circ\prime}(O/A) + U^{\circ\prime}(A/R)}{2}.$$

If, in addition:

$$U^{\circ\prime}(A/R) > U^{\circ\prime}(O/A)$$

the redox reaction of the so-called amphoteric compound, Amp, on itself, called dismutation:

$$2\,Amp + \ldots \rightleftharpoons Ox + Red + \ldots, \Delta G^{\circ\prime}_d$$

is or should be dominantly shifted at equilibrium towards the decomposition of Amp.

2.3.2. Parallel associations of redox couples.

Several redox transitions are currently possible between 2 given states of oxidation of organic compounds. This is the case, e.g., when different protona-

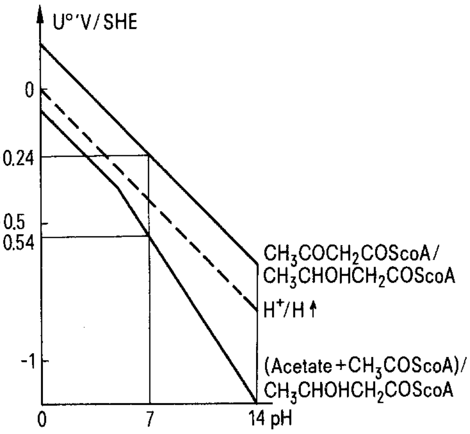
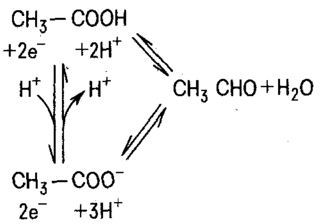


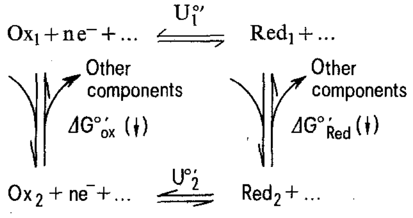
Fig. 1. Energetics of the overall oxidation of β-hydroxybutyryl CoA into acetate and acetylCoA, as: $CH_3CHOHCH_2COSCoA + H_2O \rightleftharpoons CH_3{-}CO_2H + CH_3COSCoA + 2e^- + 2H^+$ and of its oxidation into acetoacetylCoA, as: $CH_3CHOHCH_2COSCoA \rightleftharpoons CH_3COCH_2COSCoA + 2e^- + 2H^+$ (from Buvet and Le Port, and Buvet[7]).

tion states of the involved oxidation and reduction states occur, such as in:



But, at least as important for the understanding of several biochemical steps are the cases where more complex changes of bonds are involved such as in degradative oxidation of β-hydroxyacyl coA (see 3.1) or thioesterifying oxidations of aldehydes (see 3.2) or in redox couples between complexed forms of metallic cations.

For any such network of processes, represented in the most general way, by:



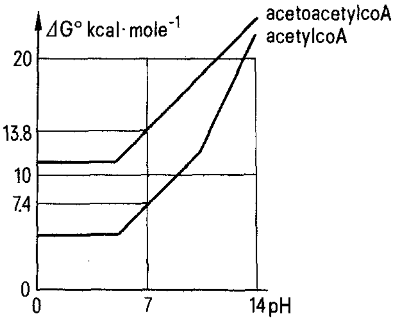


Fig. 2. Comparison, taking pH into account, of the energy liberated in the hydrolytic degradation of acetoacetylCoA as: acetoacetylCoA $+ H_2O \rightleftharpoons$ acetate + acetylCoA and used in the condensation leading to acetylCoA from acetate, through: acetate + HSCoA $\rightleftharpoons$ acetylCoA $+ H_2O$ (from Buvet and Le Port, and Buvet[7]).

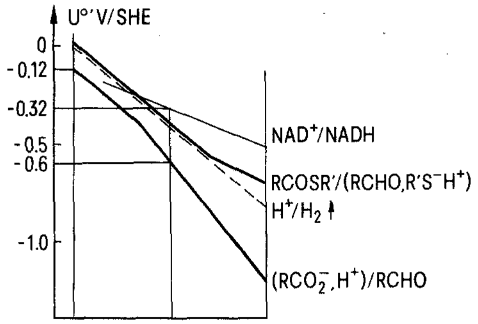


Fig. 3. Energetics of the redox processes $RCOOH + 2e^- + 2H^+ \rightleftharpoons R{-}CHO$ and $RCOSR' + 2e^- + 2H^+ \rightleftharpoons R{-}CH(OH){-}SR' \rightleftharpoons RCHO + HSR'$ (from Buvet[8]).

involving non-redox processes:

$$Ox_1 + \ldots \rightleftharpoons Ox_2 + \ldots, \Delta G^{\circ\prime}_{ox}$$

$$Red_1 + \ldots \rightleftharpoons Red_2 + \ldots, \Delta G^{\circ\prime}_{Red}$$

it is also easy to show, by considering the additivity of standard free enthalpies of the non redox reactions and of the redox reactions of both couples with any reference one, that

$$nF(U^{\circ\prime}_1 - U^{\circ\prime}_2) = -\Delta G^{\circ\prime}_{ox} + \Delta G^{\circ\prime}_{Red}.$$

3. *Kinetic criteria for the implementation of redox reactions*

From any organic compound, many electron-exchanging stoichiometric equations can be written, involving either different levels of oxidation of C-atoms to the total oxidation to $CO_2\nearrow$ or different reductions to the total one to $CH_4\nearrow$.

Considering the apparent standard potentials of all the oxidation processes, it appears very frequently that they decrease when the involved stoichiometric balance of electrons increases, i.e., that the most complete oxidation processes are energetically the easiest ones. Symetrically, the most complete reductions are in such cases the energetically easiest ones, i.e. occur at the highest potentials. Consequently all intermediate oxidation levels of carbon should undergo dismutation if complete equilibrium was reached.

However, it is well known that only redox processes involving a small number of electrons effectively occur. In this respect, the experimental facts, as well as logical evidence, lead to the consideration that two general kinetic interdiction rules limit the feasibility of redox processes.

Rule 1. No redox process, which involves at least one couple exchanging more than 2 electrons, is directly feasible, at or near its equilibrium state, i.e. near the minimal energetic requirements which should render it globally possible. The logical evidence of this rule stems from the fact that relative positioning of the molecules allowing simultaneous transfer of several electron doublets, by any proper overlapping of orbitals or tunnel effect when the reagents of both involved redox couples are in contact, cannot be conceived according to all the available concepts relating to electronic structures of molecules.

But experimental evidence shows that a 2nd kinetic rule must also be considered which forbids many mono- or bi-electronic redox couples to be implicated in intermolecular electron transfer reactions.

Rule 2. There exists neither experimental evidence nor logical reasons for considering that intermolecular electron transfers are feasible at or near their equilibrium conditions when at least 1 of the 2 implicated redox couples involves any modification of the covalent topology of its relatively heavy atoms.

In fact, this rule can be considered as a transposition to redox chemistry of the well known Franck Condon rule currently admitted in spectroscopy. Here it appears that the inertia of electrons is so small in comparison with the relatively large ones of C, O, N or S atoms, that the order of magnitude of the time intervals which are necessary for building or breaking a simple covalent linkage between 2 such heavy atoms, i.e., to change their relative positioning by more than approximately 1 Å, are very much larger than the time intervals involved in the transfer of electrons between 2 different molecules when in the best position for such a process to occur.

Consequently, redox reactions implying global kinetically forbidden redox couples, regarding both rules, should be able to occur only through pathways involving discrete sequences of kinetically permitted steps, each involved process implying its own energetic conditions for taking place.

The redox couples involved in redox reactions of these sequences are necessarily restricted to either couples exchanging simply 1 or 2 electrons or to couples exchanging 1 or 2 electrons together with protons. In the latter case, additional restrictions must be considered in connection with the energetic and kinetic mobility of electrons and protons from or to the reacting oxidant and reductant[4,5].

3.1. *Intermolecular electron transfers followed by modifications of covalent topology of heavy atoms*

The simplest biochemical examples of oxidation globally modifying the covalent topology of heavy atoms in a substrate is found in pathways implying successively a permitted intermolecular electron transfer and a non redox modification of covalent topology of heavy atoms; for instance, the oxidation of acyl coA or of succinate.

In the latter case, the redox couple which corresponds to the energetically easiest bielectronic oxidation of succinate:

$$^{-}OOC{-}CH_2{-}CH_2{-}COO^{-} + H_2O \rightleftharpoons$$
$$^{-}OOC{-}CHOH{-}CH_2{-}COO^{-} + 2\,H^{+} + 2\,e^{-};$$
$$U^{\circ\prime} = +0.012\ V/_{SHE}\ \text{at pH } 7^{6}$$

must be considered as forbidden because of the change of covalent topology it involves between the C(2) of malate and the O atom from water. In fact, it is biochemically replaced by the following sequence of:

- a permitted intermolecular electron transfer occurring near equilibrium with flavoproteins, which involves the α,β-dehydrogenation:

$$^{-}OOC{-}CH_2{-}CH_2{-}COO^{-} \rightleftharpoons$$
$$-OOC{-}CH{=}CH{-}COO^{-} + 2\,e^{-} + 2\,H^{+};$$
$$U^{\circ\prime} = +0.031\ V/_{SHE}\ \text{at pH } 7$$

and implies a higher standard potential than the globally performed oxidation;

- and, in this case, a weakly exoenergetic hydration of the ethylene bond implementing the change of covalent topology at a larger time scale:

$$^{-}OOC{-}CH{=}CH{-}COO^{-} + H_2O$$
$$\rightleftharpoons\ ^{-}OOC{-}CHOH{-}CH_2{-}COO^{-};$$
$$\Delta G^{\circ\prime} = -0.87\ \text{kcal} \times \text{mole}^{-1}.$$

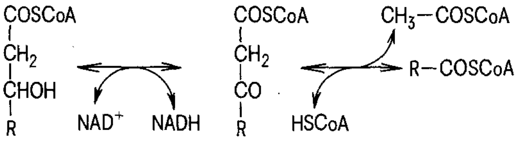
In this sequence the additional redox standard free enthalpy $\Delta G^{\circ\prime}_{add}$ which is necessarily involved in the oxidation step because of the kinetic interdiction, in excess of the standard free enthalpy balance obtained in the global oxidation:

$$\Delta G^{\circ\prime}_{add} = 2 \times 23.05\ (0.031\text{-}0.012),\ (\text{kcal} \times \text{mole}^{-1})$$
$$= +0.87\ \text{kcal} \times \text{mole}^{-1}$$

is later simply recuperated during the hydration process.

But a most important consequence of such a combination of energetic criteria and kinetic interdiction rules is the opportunity they offer for converting redox energy into other forms of chemical energy, e.g., by chemically coupling the production of a high-energy condensed derivative with the relaxation of redox energy.

This is the case, e.g., in the oxidation of β-hydroxyacyl coA which occurs in the catabolism of fatty acid chains, according to:



In this case, the energetically easiest bielectronic oxidation of the 3-hydroxyl group should involve the degradative hydrolysis of the $C_2{-}C_3$ bond, at potentials lower than those of $H^{+}/H_2\nearrow$ couple (figure 1) according to:

$$R{-}CHOH{-}CH_2{-}COSCoA + H_2O \xrightleftharpoons{2e^{-},\,3H^{+}} RCO_2^{-} + CH_3COSCoA,\ U^{\circ\prime}_{d}$$

But, since this process involves changes of the covalent topology of heavy atoms, related to the incorporation of 1 oxygen atom and to the degradation between C_2 and C_3, it is kinetically blocked.

On the other hand, the simpler bielectronic oxidation to the 3-keto derivative:

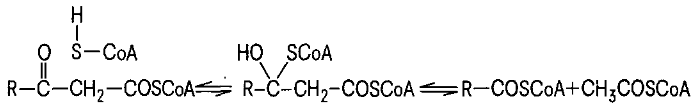
$$R{-}CHOH{-}CH_2{-}COSCoA \xrightleftharpoons{2e^{-},\,2H^{+}} R{-}CO{-}CH_2{-}COSCoA,\ U^{\circ\prime}_{k}$$

is not theoretically kinetically forbidden and can be performed by enzyme catalysis with NAD^{+}. But it occurs at higher potentials and involves investing an excess of redox standard free enthalpy, $\Delta G^{\circ\prime}_{add}$, such as:

$$\Delta G^{\circ\prime}_{add} = 2\,F\,(U^{\circ\prime}_{k} - U^{\circ\prime}_{d}),$$

which is simply the opposite of the apparent standard free enthalpy of the degradative hydrolysis of the C_2-C_3 bond of the β-keto derivative (figure 2).

This process could further ensure the relaxation of $\Delta G^{\circ\prime}_{add}$. However, this degradative hydrolysis of the C_2-C_3 bond by H_2O molecules is also kinetically very slow as is also the case with esters or other acylated condensates, although the nucleophilic attack of C=O by RS^- can occur very much more rapidly as in:



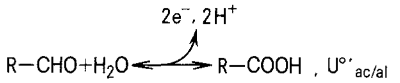
$$R-\overset{O}{\overset{\|}{C}}-CH_2-COSCoA \rightleftharpoons R-\overset{HO\ \ SCoA}{C}-CH_2-COSCoA \rightleftharpoons R-COSCoA + CH_3COSCoA$$

and leads to the recovery of a part of $\Delta G^{\circ\prime}_{add}$ into a newly formed acyl CoA (figure 2).

3.2. *Intermolecular electron transfer preceded by modifications of covalent topology of heavy atoms*

The modification of the covalent topology of heavy atoms, which occurs after intermolecular electron transfer in the formerly given pathways, can alternatively be involved before it, as far as some energetically and kinetically feasible non redox process allow it.

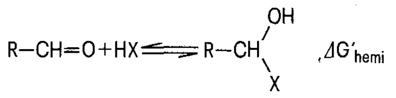
This is the case e.g., with biochemical oxidation of aldehydes. If considering only bielectronic oxidation, the energetically easiest oxidation of aldehydes should produce acids, according to the equation:



$$R-CHO+H_2O \xrightleftharpoons{2e^-,\ 2H^+} R-COOH\ ,\ U^{\circ\prime}_{ac/al}$$

at standard apparent potentials $U^{\circ\prime}_{ac/al}$, far much lower than those of $H^+/H_2\uparrow$ and nicotinamidic couples (figure 3). Nevertheless, this oxidation cannot be achieved near $U^{\circ\prime}_{ac/al}$ because it involves the formation of a new C–O bond.

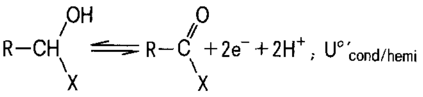
However, hemiacetalic forms of oses or hemithioacetals of simple aldehydes are formed at the equilibrium of:



$$R-CH=O+HX \rightleftharpoons R-CH\begin{matrix}OH\\X\end{matrix}\quad ,\Delta G'_{hemi}$$

where HX is either an alcohol group (conveniently located in the same molecule as the aldehyde one) or a thiol RSH, with standard free enthalpies, $\Delta G^{\circ\prime}_{hemi}$, which are near zero or even slightly negative ($\Delta G^{\circ\prime}_{hemi} = -1.8$ kcal × mole^{-1} for the addition of C_2H_5SH on CH_3CHO) and not dependent on pH below the pK_a of XH.

Consequently, the oxidation by intermolecular electron transfers of these hemiacetalic forms becomes kinetically possible, since it does not involve any more modifications of covalent topology of heavy atoms, according to the stoichiometrically simpler oxidation step:



$$R-CH\begin{matrix}OH\\X\end{matrix} \rightleftharpoons R-C\begin{matrix}O\\X\end{matrix} + 2e^- + 2H^+ ;\ U^{\circ\prime}_{cond/hemi}$$

which now produces a condensed derivative of the otherwise obtained acid, and consequently occurs at apparent standard potentials equal to:

$$U^{\circ\prime}_{cond/hemi} = U^{\circ\prime}_{ac/al} + \frac{\Delta G^{\circ\prime}_{cond} - \Delta G^{\circ\prime}_{hemi}}{2\,F}$$

where $\Delta G^{\circ\prime}_{cond}$ is the positive apparent free enthalpy of condensation of the condensate R–CO–X.

In fact, $\Delta G^{\circ\prime}_{cond}$ being more positive than $\Delta G^{\circ\prime}_{hemi}$, because the R–CO residue is more oxidized than the R–CHOH one, the redox step involved in this pathway occurs near the standard potential of the $H^+/H_2\uparrow$ couple and stores the condensation energy of R–CO–X (figure 3).

3.3. *Redox reactions occurring by molecular association followed by intramolecular electron shift*

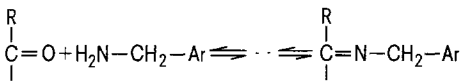
The last kind of pathway for performing a redox reaction, which globally modifies the covalent topology of heavy atoms between involved reagents and products, implies successively

a) the non redox formation of 1 single molecule from the reacting oxidant and reductant;

b) an intramolecular shift of electrons in the formed molecule;

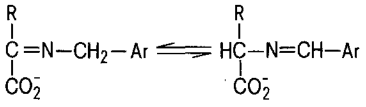
c) which is or is not followed by its breakdown into products, reduced and oxidized, respectively.

A most classical example of such a sequence occurring enzymatically at its global equilibrium and concluded by a dissociation is the aminating reduction of α-ketoacids by pyridoxamine involved in transamination. Here, an exergonic condensation first occurs, from the oxidant α-ketoacid and the reductant pyridoxamine, as:



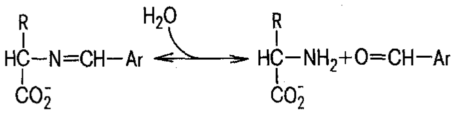
$$\overset{R}{\underset{CO_2^-}{C}}=O+H_2N-CH_2-Ar \rightleftharpoons \cdot\cdot \rightleftharpoons \overset{R}{\underset{CO_2^-}{C}}=N-CH_2-Ar$$

forming a single Schiff base molecule, wherein an electron shift arises without any change in covalent topology of heavy atoms, as:



$$\overset{R}{\underset{CO_2^-}{C}}=N-CH_2-Ar \rightleftharpoons H\overset{R}{\underset{CO_2^-}{C}}-N=CH-Ar$$

This tautomery of the Schiff base is finally completed here by hydrolysis of the new imino group, as:



$$\underset{CO_2^-}{\overset{R}{HC}}-N{=}CH-Ar \xleftrightarrow{H_2O} \underset{CO_2^-}{\overset{R}{HC}}-NH_2+O{=}CH-Ar$$

In some cases, the same process is applied from simpler reagents without any final separation into 2 products.

Particularly typical in this respect is the case of far-from-equilibrium hydroxylation of initially non oxidized C atoms, which can even occur non enzymatically in sensible positions of aromatic structures. Such reactions appear to be driven by any process having produced $HO^{\cdot}$ radicals in a previous step, e.g., from reduction of dissolved O_2 to H_2O_2 followed by any catalytic dissociation of the peroxide bond[7]. Such radicals can then attack the RH bond, as:

$$RH + {}^{\cdot}OH \rightarrow R^{\cdot} + H_2O$$

followed by:

$$R^{\cdot} + {}^{\cdot}OH \rightarrow ROH$$

or

$$R^{\cdot} + HOOH \rightarrow ROH + {}^{\cdot}OH$$

finally resulting in the global oxidation:

$$\begin{cases} RH + H_2O \rightarrow ROH + 2\,e^- + 2\,H^+ \\ H_2O_2 + 2\,e^- + 2\,H^+ \rightarrow 2\,H_2O \end{cases}$$

i.e.

$$RH + H_2O_2 \rightarrow ROH + H_2O$$

which globally performs a redox reaction involving modifications of covalent topologies of both implied reagents, without involving at any time any intermolecular electron transfer, forbidden because it proceeds too fast to be simultaneous with a change in the covalent vicinity between relatively heavy and too inert atoms.

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Electrochemical energetics of the biosphere

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1. *Energy balances involved in the building or the degradation of biochemical compounds*

Numerical data related to standard free enthalpies of formation of organic compounds from elements are available for a set of simple carbonaceous chemicals in their pure states[1]. These chemicals can be considered as roughly representative of more complex biochemicals owing to the additivity of energy balances involved in the building up of linkages which are not closely adjacent in molecules. Considering the compared order of magnitudes of energy balances involved in the formation of covalent bonds in these compounds and of their possible solution and interaction energies in aqueous phases, these numerical data, though related to the pure states of compounds, also represent a reasonable approximation of those involved in the formation of these compounds in aqueous phases in biological systems. It is well known that many of these standard free enthalpies of formation of carbonaceous chemicals from graphite and gaseous oxygen, hydrogen and nitrogen in their standard states are negative, which simply means that these compounds are energetically more stable than the elements, and that only some are positive, concerning mainly unsaturated organics, which means that even their formation from elements should involve some kind of external energy supply.

However, it must be emphasized that 3 groups of global organic syntheses always present positive free enthalpy balances near ambient temperature and pressure.

This is the case for any synthesis from the most