

Energy Sources, Self-organization, and the Origin of Life

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Abstract The emergence and early developments of life are considered from the point of view that contingent events that inevitably marked evolution were accompanied by deterministic driving forces governing the selection between different alternatives. Accordingly, potential energy sources are considered for their propensity to induce self-organization within the scope of the chemical approach to the origin of life. Requirements in terms of *quality* of energy locate thermal or photochemical activation in the atmosphere as highly likely processes for the formation of activated low-molecular weight organic compounds prone to induce biomolecular self-organization through their ability to deliver quanta of energy matching the needs of early biochemical pathways or the reproduction of self-replicating entities. These lines of reasoning suggest the existence of a direct connection between the free energy content of intermediates of early pathways and the quanta of energy delivered by available sources of energy.

Keywords Biological minimum energy quantum · Coupled reactions · Energy barriers · Free energy · Photolysis · Self-organization · Thermolysis

Introduction

Since attempts to make life initiate from scratch are likely to remain beyond the reach of science in the near future, the origin of life is one of the most stimulating questions among those in relation to the emergence of self-organization (von Kiedrowski 2001). The mere possibility of achieving this target is dependent on the reliability of the alternative between two opposite philosophical positions about the role of contingency in the process. The first one has been supported by Christian de Duve (1996) who claimed that Life is a *cosmic imperative*, whereas Jacques Monod (1970) considered that it is the result of a succession of

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highly improbable events. The latter position leaves almost no room for scientific investigation since it is meaningless to build laws from a single successful event resulting from chance only or to perform experiments with almost no possibility of success. The former one encompasses the idea that driving forces are capable of inducing simple physicochemical processes to generate self-organized sub-systems of increasing complexity.

But, it is more likely that contingency played a major role together with driving forces in inducing self-organization, which is consistent with its essential role in creating the diversity responsible—with selection—for biological evolution. Moreover, a contribution of chance is mandatory in any historical process, so that a scientific description of self-organization must involve a combination of driving forces and non-deterministic events. Self-organization in chemical systems is rooted in the discontinuity of matter at the atomic/molecular scale, but two main strategies to get macroscopic heterogeneity in molecular assemblies are available. The first one is to allow molecular building blocks to interact in a non-covalent way to give crystals or *supramolecular* structures (micelles, aggregates, and more or less precisely defined supramolecular architectures). These structures are usually under thermodynamic control since the formation of non-covalent interactions commonly involves low kinetic barriers—except when a strong interaction is the result of the cooperation of multiple weak interactions leading to entropically stabilized structures (Jencks 1981; Hunter 2009). The second one results from amplification processes, and it is revealed by the observation of molecular assemblies adopting collective dynamic behaviors, as for instance chemical waves (Biosa et al. 2006), which are reminiscent of the organization of metabolic complexity, rather than simply formed by static, ordered spatial arrangements. The development of experimental and theoretical investigations now allows the proposal of increasingly detailed scenarios for the emergence of biological organization. If we consider the description of life as corresponding to a *state of matter* driven by the dynamic stability of self-reproducing chemical systems (Eigen 1971; Eigen and Schuster 1977; Eigen et al. 1988; Pross 2005; 2009; Wagner and Ashkenasy 2009), then any energy exchange must take place at the molecular level. In chemical systems leading to the emergence of life, energy is likely to have been brought about by energy-rich molecules (chemical energy) and released in the environment as heat or inactivated waste materials. The following question that we intend to address here is to determine whether these requirements have some consequence for the nature of the chemical systems involved. This report is devoted to identify the main properties conferring to energy sources or organic energy carriers the essential features supporting the emergence of self-organizing systems based on organic molecules. Taking into account, on the one hand, the fact that exchanges of energy take place through finite quanta and irreversibility leading them to be dispersed into less concentrated forms and, on the other hand, the biological free energy requirements of purported early pathways, we recognize processes starting from thermal or photochemical lyses of gaseous species in the atmosphere as presenting the attributes needed to induce biomolecular self-organization.

Self-organization and the Second Law

The spontaneous formation of order from disorder is in contradiction with the common sense, which is expressed in thermodynamic language by the Second Law stating that entropy tends to increase in an isolated system. Then, chemical systems spontaneously evolve toward the equilibrium state in which the concentrations of chemical species are determined by their relative energy levels and statistical rules. To remain in a non-

equilibrium state, a self-organizing system must be open or at least closed (exchanging matter and energy, or energy only with its environment, respectively) (Kondepudi and Prigogine 1998), in which case, the entropy loss associated with the formation of a structure is compensated by the increase in disorder in the environment in such a way that the overall entropy increases (Schrödinger 1946; Plasson and Brandenburg 2010). It follows that exchanges of energy and/or matter are needed as a starting point for self-organization dynamics. In a locally closed system (exchanging only energy with its environment) at the steady state, the amount of energy (measured as enthalpy ΔH) that enters the system must be identical to the amount that is released, but possibly with a strong increase in entropy, i.e. requiring that energy is released under a more "diluted" form than when entering the system (this is the case for instance of the Earth, the surface temperature of which is regulated so that the solar energy received as light is compensated by radiation at longer wavelengths). This can be expressed in different terms by considering that self-organization in a closed system requires the conversion of "low entropy energy" into "high entropy energy" (usually heat).

A Minimum Quantum of Energy in Biology

Because energy flows from low-entropy resources to high-entropy waste, not all forms of energy can be integrated into a metabolism. This is a direct consequence of the Second Law that makes the formation of high-energy species unlikely by assembling the content coming from two (or more) different reactants, which does not completely avoid the transient formation of high-energy intermediates provided that their steady-state concentration does not exceed the equilibrium value from reactants. These observations are in relation with the proposition that the amount of energy available per individual chemical event must exceed a threshold to be integrated into the metabolism of living organisms (Schink 1997; Hoehler 2007). The value of that threshold is the direct consequence of the main process used in cells to exploit energy through the ATPase-dependent production of ATP by chemiosmosis (Mitchell 1961) by means of the translocation of protons across the membrane. Since several discrete events are needed to synthesize a single ATP molecule, the minimal quantum of energy represents ca. 1/3 of ATP free energy content under physiological conditions (ca. 20 kJ mol⁻¹). Being dependent on the process by which energy is collected, this limit has very probably changed in the course of evolution and was certainly different earlier than the advent of the highly complex mechanism of chemiosmosis. Before trying to give an assessment of its earlier value, it is worth to notice that we can predict that it should have decreased during evolution. The need for making more and more energy available for their metabolism must indeed have driven the evolution of living organisms toward the possibility of collecting lower quanta of free energy. In addition, we can also try to detect in contemporary biochemical pathways a remnant of the early value that was needed to induce biological self-organization. To this aim, the free energy of several biochemical processes corresponding to the hydrolysis of activated acyl or phosphoryl intermediates, which are likely to have been already present in early organisms, is displayed in Table 1. It appears that there is a cluster of essential biochemical processes with standard free energy changes in the range 50–70 kJ mole⁻¹, mostly essential at early stages, which include the formation of the activated intermediates of protein biosynthesis (e.g. aminoacyl adenylates) and those of the main energy metabolisms (e.g. phosphoenol pyruvate). Consistently with the previous discussion of the consequences of the Second Law, we make here the reasonable hypothesis that the early minimum quantum of energy that could be integrated in these

Table 1 Standard free energy of hydrolysis of common biochemical intermediates / functional groups at pH 7 and 25°C

	ΔG° / kJ mol ^{-1a}
Alkyl ester	-20
Acetyl coenzyme A (thioester)	-31
ATP (to ADP & Pi)	-31
ATP (to AMP & PPi)	-45.6 ^b (-32)
Pyrophosphate (PPi)	-19.2 ^b
Aminoacyl-tRNA (amino acid ester)	-35
Glycine ethyl ester	-35
Acetyl phosphate	-43
Amino acid thioester	ca.-47
Aminoacyl phosphate	ca.-50
Carbamoyl phosphate	ca.-51
Acetyl adenylate	-55
Phosphoenolpyruvate	-62
Aminoacyl adenylate	-83.6 ^c (-70) ^d

^a From Jencks (1976) unless otherwise mentioned; ^b Revised value published considering new data for pyrophosphate hydrolysis (Frey and Arabshahi 1995), but the original one has been mentioned here in brackets since it is consistent with the scale determined for acyl group transfer that includes thioesters and adenylates; ^c From Wells et al. (1986) and taking into account the revised value for ATP (Frey and Arabshahi 1995). ^d Original estimate of Wells et al. (1986) calculated using the earlier value for ATP (Jencks 1976). See Appendix

essential pathways of an early metabolism was reaching or exceeding this value. It is also important to mention that some of these high-energy intermediates were not initially accessible in significant concentration from ATP. This is the case for example for aminoacyl adenylates, with an equilibrium constant of formation from ATP and free amino acid of ca. $3.5 \cdot 10^{-7}$ (Wells et al. 1986),¹ which makes the evolutionary process through which these intermediates have been selected highly problematic, starting from ATP, and then questions the initial role of ATP as a universal energy carrier (Pascal et al. 2005).

Chemical Energy Sources

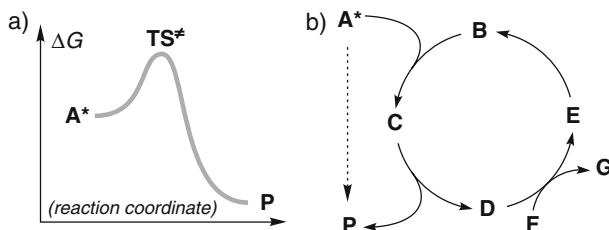
For energy to be available any source of chemical energy or energy carrier alternative to ATP must correspond to a system in which reactants and products are present in far from equilibrium concentrations. In this way, stepwise chemical processes can give rise to more or less complicated products. However, a chemical source of energy or a free energy carrier must additionally be present in a metastable state for energy to be stored over sufficient periods of time. Accordingly, it can be defined as *a reactant (or a system of reactants) in*

¹ In present day living organisms, pyrophosphate hydrolysis is used to drive aminoacyl adenylate formation to completion so that the later takes advantage of the free energy corresponding to the hydrolysis of both phosphoanhydride bonds of ATP. But a similar prebiotic (or early biological) adenylating pathway seems highly unlikely since it would have required a pyrophosphatase (or a chemical analogue) efficient for pyrophosphate hydrolysis while remaining completely devoid of activity towards the structurally similar phosphoanhydride bonds of ATP.

far from equilibrium concentration with respect to products and protected from spontaneous deactivation (isolated from products) by a kinetic barrier (Scheme 1a). Although it is less obvious than the need for a free energy difference compared to product, the presence of a kinetic barrier is essential in avoiding a spontaneous breakdown into products. This barrier lets a sufficient lifetime for useful competing reactions to take place and especially coupled reactions in which the free energy of the carriers is not directly exhausted as heat but used to activate a reactant. A highly relevant possibility is that of catalytic or autocatalytic cycles that can arise when a cyclic network of reacting intermediates is present (Scheme 1b) (Morowitz et al. 2000; Shapiro 2006; Blackmond 2009). It is important to emphasize that no catalysis of a single chemical step is needed, but that catalysis is the mere consequence of the cyclic architecture of the reaction network (Eigen and Schuster 1977). Since there is no possibility of having a stationary state with two different autocatalysts coexisting at the expense of a single energy source (Lifson 1997), then a selection based on the most efficient network of replicating molecules can conceivably take place. These views are consistent with the importance of the circumvention of chemical barriers in inducing self-organization (Eschenmoser 1994; 2007). In principle, selection acting on the ability to exhaust the source of energy (the function) would be independent of the fact that replicating species consist of either small molecules (Shapiro 2006) or genetic polymers (capable of imperfect copying—mutations—and thus possibly of improvement), with the nevertheless highly significant exception that in the latter case, an open-ended evolution process might be initiated (Pross 2005; 2009; Vasas et al. 2010).

Thermal Energy and Photochemistry

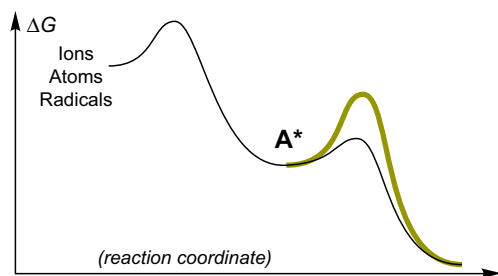
If we consider that energy transfer at the atomic or molecular scale is a physical process that takes place through the exchange of quanta and not in a continuous way, we can look for physical processes capable of providing amounts corresponding to free energy changes needed to initiate the main biochemical processes (assumed to be equal to or exceeding the range 50–70 kJ mol⁻¹). The most obviously present physical forms of energy on the early Earth are thermal energy and light. The conversion of light from the Sun with a maximum of emission in the visible part of the spectrum (400–800 nm) resulting from a surface



Scheme 1 **a** A free energy source / carrier A^* must be protected from spontaneous deactivation by a kinetic barrier. **b** Illustration of potential catalytic or autocatalytic cycles resulting from coupled reactions of an energy carrier A^* that can depart it of spontaneously reacting into P as in (a) directly or through an (or several) intermediate(s) C . Catalysis refers to the increase in the rate of consumption of the carrier A^* . In this scheme, compounds B , D , or E can be considered as catalysts simply because they are regenerated by the cyclic network (Eigen and Schuster 1977). Autocatalysis may arise if the product G (or any further downstream product resulting from G) is identical to one of the intermediates of the catalytic loop (B , D , or E) so that their concentrations (as catalysts) may geometrically increase as reaction proceeds

temperature of ca. 6000°K would be able to provide energy quanta (150–300 kJ mol⁻¹ expressed at a molar scale) exceeding the range of biochemical events. The requirement for thermal energy is less obvious to express in terms of exchange of quanta of energy because of the difficulty of converting thermal energy into other forms of energy but, as for sunlight, the spontaneous process can be characterized considering the black-body radiation. Then, the range 50–70 kJ mol⁻¹, considered above as crucial for essential metabolic processes, may be brought about as a result of the maximum of emission of a solid at 1200–1700°K. This means that the corresponding chemical energy can hardly be obtained from a direct spontaneous irreversible transfer on the Earth. On the other hand, thermal energy can be *partly* converted into other forms of higher quality by a natural heat engine as a part of a thermodynamic cycle requiring a heat source and a cold sink. This is the case for example of atmospheric processes inducing lightning, which may alternatively be considered as an independent energy source for prebiotic chemical processes. But the possibility that biochemical pathways involving the most activated intermediates of Table 1 emerged as a direct result of a proto-biochemical heat engine (Muller and Schulze-Makuch 2006) seems unlikely because (i) of the complexity needed for this kind of systems, (ii) of the inability to reach the free energy range required, (iii) of the absence of living organisms presently using this kind of metabolic pathway, and (iv) of the above mentioned direction of evolution towards lower values for the smallest energy quantum in biology. Anyway, the range 50–70 kJ mol⁻¹ is less than one order of magnitude lower than the amount needed to break univalent chemical bonds, ca. 400 kJ mol⁻¹. Then some compounds resulting from photolysis or thermolysis can be expected to correspond to the requirement provided that the recombination of lysis products takes place away from the activation source. As a result, processes capable of providing energy for biochemical organization may be found in lightning (heating transiently the atmosphere up to a few tens of thousands of K) or from photochemistry. The process of formation of low-molecular weight organics by recombination of ions and radicals generated by photolysis or thermolysis induced by lightning is likely to generate some intermediates with significant lifetimes (Scheme 2). The advantage of these processes in generating chemical species is that they involve a very short activation period followed by a fast quenching so that recombination can take place in a cooled environment efficient in preserving those species constrained in a free energy well by kinetic barriers (Scheme 2) (Eschenmoser 1994; 2007). Energy carriers formed in this way may have lifetimes long enough to reach the Earth's surface or a place in which they can sustain the development of a metabolism.

In Table 2 are presented the values of the free energies of hydrolysis of some low-molecular weight compounds calculated from literature data. It is worth to notice that



Scheme 2 Intermediates generated by recombination of lysis products correspond to the definition of energy carriers provided that the height of the kinetic barrier of their spontaneous decomposition is sufficient

Table 2 Standard free energy of reaction (hydrolysis unless otherwise mentioned) of potential prebiotic energy-rich low-molecular weight compounds at pH 7 and 25°C

Reactants	Products	ΔG° / kJ mol ⁻¹ ^a
HC≡CH (g)	Acetaldehyde (aq)	-111.8
Alanine nitrile (aq)	Alanine (aq)+NH ₃ (aq)	-80.6
HC≡N (aq)	HCO ₂ ⁻ +NH ₄ ⁺	-75.6
N=C=O ⁻	HCO ₃ ⁻ +NH ₃ (aq)	-54.5
Urea (aq)	HCO ₃ ⁻ +NH ₄ ⁺ + NH ₃ (aq)	-28
S=C=O (g)	CO ₂ (aq)+H ₂ S (aq)	-16.9
FeS (s)+H ₂ S (aq)	FeS ₂ (s)+H ₂ (g)	-31

^a Determined from literature data (see [Appendix](#))

activation in upper layers of the atmosphere (as well as in space), merely as a result of the very dry environment, is likely to favor the formation of organic derivatives in a dehydrated state compatible with a subsequent delivery of energy by hydrolysis upon transfer into liquid water. Some of these molecules containing double or triple covalent bonds are able to supply a substantial amount of free energy upon hydrolysis. It can be observed from the values displayed in Table 2 that the low-molecular weight molecules involving CC (acetylene) and CN (α -aminopropionitrile, hydrogen cyanide) triple bonds can in principle sustain the formation of all important biochemical intermediates of Table 1. This ability may be extended to many other species formed through reducing atmosphere activation or found in the interstellar media (Guillemin et al. 2004; Thaddeus 2006) that include these functional groups such as other aminonitriles (Lazcano and Miller 1999; Pascal et al. 2005), cyanamide, or cyanoacetylene. It is worth noting that sparkling neutral atmospheres also produces amino acid precursors (Cleaves et al. 2008) together with oxidized nitrogen species that are able to deliver energy to the system as well (Commeyras et al. 2004). By comparison, the inorganic process leading to pyrite and claimed to be able to give rise to a protometabolism in hydrothermal systems (Wächtershäuser 1988) is unable to lead to the formation of the essential biochemical intermediates of Table 1 in a favorable way for free species in solution in the absence of further thermodynamic stabilization. Another low-molecular weight organic molecule, formaldehyde, important as a chemical starting material for several abiotic synthetic processes and in principle able to release energy by hydration in its dehydrated state, has not been mentioned in Table 2 because of the fast kinetics of the hydration process (Bell and Evans 1966) that does not fit the kinetic barrier requirement. However, in addition to hydrolytic transformations and processes indicated in Table 2, other reactions derived from the reactivity of formaldehyde and similar species could be considered as resources of energy. This is the case for example of the transformations of aldehydes and ammonia into amino acid thioesters intermediates promoted by thiols (Wieland et al. 1955a; Weber 1998) in agreement with the high chemical potential of sugars through redox disproportionation (Weber 2000). Moreover, a direct contribution of photochemistry to early metabolisms seems to be achievable for example through the photochemically assisted and uracil-catalyzed formation of acetyl phosphate from thioacetate recently described by Hagan (2010). Acetyl phosphate formed in this way could be sufficient to drive many protometabolic processes, but the comparison of free energy potential displayed in Table 2 makes the formation of aminoacyl adenylates unlikely from simple acyl phosphates. It is tempting to suggest that substituting thioacetate

for α -amino thioacids in this photochemical process might in principle lead to activated thioesters or disulfides that have already been observed (Wieland et al. 1955b; Weber 2005; Maurel and Orgel 2000) to yield α -amino acid *N*-carboxyanhydrides intermediates, which are within the 50–70 kJ mol⁻¹ range considered here (Pascal et al. 2005) and can act as aminoacyl adenylate precursors (Biron et al. 2005; Leman et al. 2006).

Conclusion

This discussion was intended to demonstrate that it is possible to get new insights by encompassing both the representation of life as a state of matter governed by the dynamic stability of self-reproducing systems (autocatalytic loops, replicators) and the free energy requirements of early biochemical processes. It allows building scenarios of life's emergence in which every step is under the control of a driving force acting in selecting, among the variety of reproducing components arising as a result of independent (contingent) events, those whose population increases faster in an environment constrained by the availability of matter and energy sources. Considering that present day biochemistry conserve some of the essential intermediates that were present in early living organisms allows to identify the upper range in which early biochemical energy transfer were working at those times. We have proposed here that only a certain kind of chemistry could feed these biochemical processes through coupled reactions and metabolic cycles. This proposal, consistent with the idea that early organisms were unable to concentrate energy at the molecular level (operating a kind of thermodynamic engine) but depended on spontaneous energy flows, results in a correspondence of the free energy quanta exchanged in biochemical pathways with the requirements in terms of the quality of the supply in energy. However, these views present a limitation because usual metabolic cycles do not present the variability needed for a non-limited accumulation and storage of information, which has given support to criticism (Orgel 2008). In contrast, this limitation would not have been present with systems that involve genetic polymers capable of accumulating information in their sequence though their replication obeys specific features (von Kiedrowski 1986; Szathmáry and Gladkih 1989; Szathmáry and Maynard Smith 1997; Szathmáry 2000). Anyway, and independently of the debate upon whether metabolic or genetic features were essential for life emergence, in the case of genetic replicators, energy is also needed to form activated monomers from simpler precursors. The possibility that activated ribonucleotides may have been formed through stepwise downhill processes from low-molecular weight precursors has received some grounds (Powner et al. 2009). But, the process may be greatly improved by the assistance of a larger metabolic network having a wider scope of chemical abilities and cooperating with genetic polymers to increase the availability of energy for the replicating system in a way consistent with the ideas developed by Gánti (2003). Experimental indications that peptide precursors such as α -amino acid *N*-carboxyanhydrides are capable of activating nucleotides have indeed been reported (Pascal et al. 2005; Biron et al. 2005). The driving forces for the emergence of life would anyway include the availability of energy for the self-organizing system in quantity and *quality* sufficient to feed the metabolism and especially to deliver quanta of energy able to provoke the formation of the key activated intermediates needed for the amplification of the whole network. Lastly, these observations are consistent with the idea that there is no fundamental difference in the driving force that was responsible for the emergence of the first features of life and its further evolution through the Darwinian process (Pross 2009).

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Appendix

Free energy calculations The free energy values were calculated from literature data as indicated in Table 3.

ATP. The value reported in the Jencks's review (1976) for the breakdown of ATP into AMP and pyrophosphate is no longer accepted in recent textbooks because of a new calculation based on a thermodynamic cycle and on a direct determination of the value for pyrophosphate hydrolysis (-19.2 instead of ca. -33 kJ mol^{-1}) (Frey and Arabshahi 1995). However, both the new determination and the earlier value (in brackets) have been reproduced in Table 1 for the following reasons.

- Most values indicated in Table 1 relate to acyl group derivatives. They have been determined either from equilibria involving activated esters or thioesters or taking into account the earlier value for ATP.
- The choice of the revised value for ATP (-45.6 kJ mol^{-1}) leads to a huge value for aminoacyl adenylates (-83.6 kJ mol^{-1}) taking into account the equilibrium constant experimentally determined by Wells et al. (1986). No easy chemical explanation can be found for this value.
- The revised value for ATP leads to a discrepancy when comparing the hydrolysis of ATP into ADP+inorganic phosphate ($\Delta G^{\circ} = -31$ kJ mol^{-1}) vs. AMP+pyrophosphate ($\Delta G^{\circ} = -45.6$ kJ mol^{-1}) for which no simple chemical explanation is available since the products have a similar state of ionization at pH 7.

Table 3 Standard free energies of formations and pK_A values used for the calculation of the ΔG° values reported in Table 2

Species (physical state)	$\Delta_f G^{\circ} / \text{kJ mol}^{-1}$	
HCN (aq)	119.66 ^a	
CN ⁻	172.38 ^a	
H ₂ O (l)	-237.18 ^a	
HO ⁻	-157.30 ^a	
HCO ₂ ⁻	-350.88 ^a	
NH ₄ ⁺	-79.45 ^b	$pK_A(\text{NH}_4^+) = 9.3$
NH ₃ (aq)	-26.71 ^a	
Urea (aq)	-202.8 ^b	
CO ₃ ²⁻	-527.815 ^b	$pK_A(\text{HCO}_3^-) = 10.25$
HCO ₃ ⁻	-586.77 ^b	$pK_A(\text{H}_2\text{CO}_3) = 6.35$
NCO ⁻	-97.41 ^a	$pK_A(\text{HNCO}) = 3.5$
HCCH (g)	209.9 ^c	
CH ₃ CHO (aq)	-139 ^b	
Alanine (aq)	-371.0 ^b	
Alanine nitrile (aq)	144.4 ^d	
COS (g)	-165.64 ^a	
H ₂ S (aq)	-27.92 ^a	$pK_A(\text{H}_2\text{S}) = 7.05$
FeS (s)	-100.77	
FeS ₂ (s)	-160.22	

^a From Amend and Shock (2001);

^b From Alberty (1998);

^c From Lide (2008); ^d Calculated taking into account the value $K = 2700 \text{ M}^{-1}$ for the equilibrium constant of formation of alanine nitrile from acetaldehyde, cyanide and ammonia reported by Béjaud et al. (1976):

$K = \frac{[\text{alanine nitrile}] [\text{HO}^-]}{[\text{acetaldehyde}] [\text{CN}^-] [\text{NH}_3]}$

An *experimental* determination of the free energy of hydrolysis of ATP into AMP and pyrophosphate would therefore be welcome to confirm the revised value.

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