A Prebiotic Surface Catalysed Photochemically Activated Synthesis of L-Cystine

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Abstract: - Alkynes such as ethyne form weak charge-transfer, \( \eta^2 \)-alkynyl complexes with surface catalysts such as Mg.porphin in which the alkynyl group is positively charged and the porphin has a negative charge. The enthalpy change is \(-0.018\) h. Rate limiting reaction with ammonia leads to addition and ring closure to form a bound Mg.aziridinyl.porphin complex. Addition of disulphide anion to the complex allows the formation of Mg.1,N-2-disulfanyl ethanimin-1yl.porphin. When the imine is bound to a Mg.porphin complex in which carbon monoxide has been oriented by exciting radiation an aziridine-2-one complex is formed hydrolysable to the amino acid 2-amino-3-disulfanyl propanoic acid. This may then act as a nucleophilic reactant with another Mg.aziridinyl.porphin complex, leading to ring opening and an imine containing an S-S bond. When this process is repeated that the imine is bound to a Mg.porphin complex in which carbon monoxide has been oriented by exciting radiation an aziridine-2-one complex is formed hydrolysable to the amino acid L-cystine.

The reactions have been shown to be feasible from the overall enthalpy changes in the ZKE approximation at the HF and MP2 /6-31G* level.

Key-Words: Ethyne, Aziridine complexes, Mg.porphin, Disulfide, L-cystine.

1 Introduction

L-cystine, \([R-(R^*,R^*)]-3,3'-dithiobis[2-amino propanoic acid]\) with \(pK_a\)s of 1.1, 2.1, 8.02 and 8.71 [2] it is widely distributed in protein, such as keratin, the protective protein of hair, wool, horn and epidermis [3]. It is formed by the dimerization of two cysteines, through the sulphur [4]. These disulfide bridges occur both within and between polypeptides; often found in extracellular proteins [5]. Natural cystine is L [1], and the organic synthesis has been described [4]. It is formed in the body from cysteine [6]. From a prebiotic perspective [7] it is desirable if the reactant molecules formed spontaneously from a supposed prebiotic atmosphere to be inevitably present. It has often been held that the atmosphere of the Earth was originally mildly reducing [1,8] implying the presence of concentrations of carbon monoxide, ammonia, water, hydrogen and hydrogen sulfide. It is also supposed that alkynes such as acetylene [9-10] were present as found on Titan, a moon of Saturn [11]. It has also been demonstrated that porphin may act as a catalyst for the formation of sugars [12] and polyenes [13].

This paper proposes a model for the catalytic photochemically activated formation of L-cystine from the gases, acetylene, carbon monoxide, hydrogen, disulfide anion, water and the catalyst magnesium porphin. An experimental gaseous mixture subjected to discharge has also produced the related amino acid methionine [14].

2 Problem Formulation

The computations tabulated in this paper used the GAUSSIAN98 [15] commercial package. The standard calculations at the HF and MP2 levels including zero-point energy corrections [16], together with scaling [17], using the same basis set, 6-31G*, are as previously published [7]. Enthalpy changes at the MP2 level not including scaled zero point energies are designated as \(\Delta H_{MP2}\). The charge transfer complexes are less stable when calculated at the Hartree Fock level [16]. If the combined energy of the products is less than the combined energy of the reactants it may show that the reaction is also likely to be spontaneous at higher temperatures. This paper uses the atomic unit of energy, the hartree [15].

\[
1\text{h} = 627.5095\text{ kcal.mol}^{-1}, \\
1\text{h} = 4.3597482 \times 10^{-18}\text{ J}
\]
Problem Solution

3.1 Total Energies (hartrees)

Mg.porphin is a powerful catalyst able to form charge transfer complexes with a number of different kinds of molecules [18]. With acetylene the ligand is positively charged (0.08) and the porphin has a negative charge. The acetylene sets as ligand with a linear H-C≡C-H structure as shown.

\[
\text{Mg.porphin + H-C≡C-H \rightarrow Mg.1,ethynyl .porphin}
\]

(1) \hspace{2cm} (2) \hspace{2cm} [1]

\[\Delta H = -0.01807 \text{ h}\]

The total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for this molecule and the others involved in the synthesis are given in Table 1.

Table 1

| Molecule                              | MP2 hartree | ZPE (HF) hartree |
|---------------------------------------|-------------|-----------------|
| Mg.porphin (1)                        | -1185.12250 | 0.29262         |
| Mg.1,ethynyl.porphin (2)              | -1262.20848 | 0.32333         |
| L-2-amino 3-disulfanyl propanoic acid (3) | -1117.46970 | 0.10877         |
| cystine (4)                           | -1439.62255 | 0.21754         |
| ethanimine (5)                        | -133.49001  | 0.07392         |
| vinylamine (6)                        | -133.46732  |                 |
| Mg.1,cis 2-amino ethenyl.porphin (7)  | -1318.54885 | 0.36958         |
| Mg.1,trans 2-amino ethenyl.porphin (8) | -1318.53002 | 0.36860         |
| Mg.1,2-amino ethylidene.porphin (9)   | -1318.50125 | 0.36526         |
| Mg.1,1H-aziridin-2-yl.porphin (10)    | -1318.55322 | 0.37028         |
| Mg.1,N-2-disulfanyl methanyl 1H-aziridine-3-one-1-yl.porphin \(^{-}\) (19) | -2226.35876 | 0.36407         |
| CO                                   | -113.02818  | 0.00484         |
| H\(_2\)                              | -1.14414    | 0.01034         |
| OH\(^-\)                             | -75.51314   | 0.00885         |
| H\(_2\)O                             | -76.19685   | 0.02298         |
| NH\(_3\)                             | -56.35738   | 0.03529         |

3.2 The overall stoichiometry for the formation of L-cystine.

In the synthesis proposed here, there are two separate sequences.

In the first, a cystine precursor is formed, 2-amino 3-disulfanyl propanoic acid, as follows, from acetylene, ammonia, disulfide anion, carbon monoxide and water, represented as,

\[
\text{H-C≡C-H + NH}_3 + \text{S-S}^- + \text{CO} + \text{H}_2\text{O} + \text{H}^+ \rightarrow \text{H}_2 + \text{C}_3\text{H}_6\text{NO}_2\text{S}_2
\]

\[\Delta H = -0.876293 \text{ h}\]

The enthalpy change is negative indicating that there may be energetically favourable routes to the formation of this amino acid precursor.

In the second sequence, the cystine precursor, L-2-amino 3-disulfanyl propanoic acid, is used as a reactant in a further set of reactions from acetylene, ammonia, carbon monoxide, hydrogen and water represented as,

\[
\text{H-C≡CH + NH}_3 + \text{C}_3\text{H}_6\text{NO}_2\text{S}_2^- + \text{CO} + \text{H}_2\text{O} + \text{H}^+ \rightarrow \text{H}_2 + \text{C}_6\text{H}_12\text{N}_2\text{O}_4\text{S}_2
\]

\[\Delta H = -0.635941 \text{ h}\]
The enthalpy change is again negative indicating that there may be energetically favourable routes to the formation of the amino acid, L-cystine. Each of these sequences will be given separately.

### 3.3 The formation of the cystine precursor, L-2-amino 3-disulfanyl propanoic acid

Although Mg.porphin is here taken as the catalyst for the reaction, the overall stoichiometry of the ammoniation of alkynes can be represented for the case of acetylene as follows [19-22],

\[ \text{H-C≡CH} + \text{NH}_3 \rightarrow \text{CH}_3\text{-CH=NH} \]  \[ \Delta H = -0.05767 \text{ h} \]  \[ (5) \]  \[ [4] \]

where ethanimine is marginally stable with regard to vinylamine and ethylene imine.

\[ \text{CH}_2\text{-CH-NH}_2 \rightarrow \text{CH}_3\text{-CH=NH} \]  \[ \Delta H_{(MP2)} = -0.02269 \text{ h} \]  \[ (6) \]  \[ [5] \]

The intermediates by which this stoichiometric reaction may have occurred are as follows:

### 3.4 The ammoniation of the Mg.1,ethynyl.porphin.

The positively charged ligand can react with ammonia to form a cis and a trans complex as follows,

\[ \text{cis Mg.1,2-amino ethenyl.porphin} \rightarrow \text{Mg.1,2-amino ethenyl.porphin} \]  \[ (7) \]  \[ (8) \]  \[ [6] \]

\[ \Delta H = 0.04471 \text{ h} \]

The potential energy diagram for the first prototropic shift is shown in Fig.1.

### 3.5 The formation of Mg.1,2-amino ethylidene.porphin.

The cis Mg.1,2-amino ethenyl.porphin may be transformed by a protropic shift to form Mg.1,2-amino ethylidene.porphin.

\[ \text{cis Mg.1,2-amino ethenyl.porphin} \rightarrow \text{Mg.1,2-amino ethylidene.porphin} \]  \[ (7) \]  \[ (9) \]  \[ [8] \]

\[ \Delta H = 0.04375 \text{ h} \]

The formation of these complexes is the rate determining step in this sequence of reactions. The cis Mg.1,2-amino ethenyl.porphin complex is the more stable and enables a close proximity of the amine group and the methine carbon atoms of the bound acetylene.
The potential energy surface for the prototropic shift on molecule, cis Mg.1,2-amino ethenyl.porphin. The X-axis depicts the bending of the angle (110.0 - A) degrees, where A is the angle H-N-C(2). The Y-ordinate represents the stretching of the single H-N bond. The minimum for the cis Mg.1,2-amino ethenyl.porphin is at X=0.0 degrees, Y=1.0 A. A saddle point is at X=65 degrees, Y=1.7 A. The minimum for the Mg.1,2-amino ethylidene.porphin is at X=80 degrees, Y=1.8 A. The energy is -1313+E h.

The activation energy for the amino group to dissociate a proton and to reach the saddle point is given as 0.049 h, whilst the activation energy to open the final aziridine ring is given as 0.041 h.

3.6 The formation of the Mg.1,1H aziridin-2-yl. porphin

The Mg.1,2-amino ethylidene.porphin undergoes ring closure to form Mg.1,1H aziridin-2-yl. porphin.

\[
\text{cis Mg.1,2-amino ethenyl.porphin} \rightarrow \text{Mg.1,1H aziridin-2-yl. porphin.} \quad (7)
\]

\[
\text{Mg.1,1H aziridin-2-yl. porphin.} \quad (10) \quad [9]
\]

The enthalpy change for the ring closure of the cis Mg.1,2-amino ethenyl.porphin complex is favourable.

\[
\Delta H = -0.00374 \ h
\]

The complex appears stable with normal bond lengths. An optimised model of the structure is shown in Fig.2.

The total energy of the The Mg.1,2-amino ethylidene.porphin is larger than the energy of the saddle point, so that the activation energy to close the ring is very low, given at the HF level as 0.001 h, whilst the activation energy to open the ring is given as 0.022 h. Therefore, the formation of Mg.1,1H aziridin-2-yl. porphin is probably a concerted reaction.

3.7 The formation of Mg.1,1-amino-2-disulfanyl ethan-1-yl. porphin

Sulfur occurs to the extent of 0.052 % in the Earth’s crust [23] and often occurs in the elemental form at volcanoes. The source of the disulfide anion is here taken to arise from the reaction of elemental sulfur with alkaline sulfide solution [23], as,

\[
\text{S} + \text{S}^- \rightarrow \text{S-S}^- \quad (11) \quad (12) \quad (13) \quad [10]
\]

\[
\Delta H = -0.26040 \ h
\]

The reaction appears to be energetic and polysulfides are known [23].

The disulfide anion may act as a nucleophilic reagent with the Mg.1,1H aziridin-2-yl. porphin,

\[
\text{Mg.1,1H aziridin-2-yl. porphin} + \text{S-S}^- \rightarrow \]
The activation energy to open the ring is calculated as, 0.000 h, whilst that to establish the ring is 0.10520 h.

3.8 The formation of Mg.1,N-2-disulfanyl ethanimin-1-yl. porphin⁻.
The Mg.1, 1-amino-2-disulfanyl ethan-1-yl. porphin⁻ reacts with any protons to form Mg.1,N-2-disulfandiyl ethanimin-1-yl. porphin⁻.

\[
\text{Mg.1,1-amino-2-disulfanyl ethan-1-yl. porphin⁻} + H^+ \rightarrow H_2 + \text{Mg.1,N-2-disulfanyl ethanimin-1yl. porphin⁻}
\]  

\[\Delta H = -0.19569 \text{ h} \]  

3.9 The formation of the 2-disulfanyl ethanimine⁻.
The final dissociation of the Mg.porphin and 2-disulfanyl ethanimine complex would require heat.

\[
\text{Mg.1,N-2-disulfanyl ethanimin-1yl. porphin⁻} \rightarrow \text{Mg.porphin} + 2\text{-disulfanyl ethanimine⁻}
\]  

The enthalpy change is,

\[\Delta H = 0.04647 \text{ h} \]  

This is the imine precursor to the amino acid L-cystine.

3.10 The formation of the Mg.1,N-2-disulfanyl ethanimin-1yl.porphin.CO⁻
The Mg.1,N-2-disulfanyl ethanimine-1yl.porphin⁻ should react with excited carbon monoxide to form an aziridin-2-one complex [12], which has been selected by the excitation of the Mg.porphin.CO complex.[12], as shown,

\[
\text{Mg.porphin} + \text{CO} \rightarrow \text{Mg.porphin.CO} \]  

\[\Delta H = 0.21136 \text{ h} \]  

\[
\text{Mg.porphin.CO} + 2\text{-disulfanyl ethanimine⁻} \rightarrow \text{Mg.1,N-2-disulfanyl ethanimin-1yl.porphin.CO⁻}
\]  

\[\Delta H = -0.21094 \text{ h} \]  

3.11 The Formation of Mg.1,N-2-disulfanyl methanyl 1H-aziridine-3-one-1-yl.porphin.
The Mg.1,N- 2-disulfanyl ethanimin-1yl.porphin.CO⁻ may easily rearrange to form Mg.1,N-2-(disulfanyl methanyl) 1H-aziridine-3-one-
1-yl.porphin’, with an activation energy of 0.135 h and a ring dissociation energy of 0.128 h.

\[ \text{Mg.1,N-2-disulfanyl ethanimin-1yl.porphin.CO}^- \rightarrow \text{Mg.porphin}^- + \text{L-2-amino-3-disulfanyl propanoic acid}. \]  

\[ \Delta H = -0.02178 \text{ h} \]

Such a complex has been inferred as able to polymerise to protein.

3.12. The Formation 2-amino-3-disulfanyl propanoic acid.
Hydrolysis in the environment of the complex, is here depicted as releasing the undissociated carboxylic acid, Fig.3, from the catalyst. Further formation of the zwitterion may occur.

\[ \text{Mg.1,N-2-(disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin}. \]  

\[ \Delta H = -0.02382 \text{ h} \]

In the second sequence of entirely analogous reactions, the cystine precursor, 2-amino 3-disulfanyl propanoic acid, acts as a nucleophilic reagent. The energies for these compounds are given in Table 2.

### Table 2

| Molecule                                                                 | MP2 Hartree | ZPE (HF) Hartree |
|--------------------------------------------------------------------------|-------------|-----------------|
| Mg.1,N-2-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl.porphin | -2436.0887  | 0.47218         |
| Mg.1,N-2-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl.porphin (22) | -2435.50986 | 0.46325         |
| Mg.1,N-2-amino 3-carboxypropan 1-disulfanyl ethanimine. (23)              | -1250.35471 | 0.17567         |
| Mg.1,N-2-amino 3-carboxypropan 1-disulfanyl ethanimine. porphin.CO (24)   | -2548.47799 | 0.47337         |
| Mg.1,N-2-(2-amino-3-carboxypropan-1-disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin | -2548.50530 | 0.47307         |

3.13. The formation of Mg.1, 1-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl. porphin.
The 2-amino-3-disulfanyl propanoic acid anion may act as a nucleophilic reagent with the Mg.1,N-1H aziridin-2-yl. porphin,

\[ \text{Mg.1,N-1H aziridin-2-yl. porphin} + \text{C}_3\text{H}_6\text{NO}_2\text{S}_2^- \rightarrow \text{L-2-amino 3-disulfanyl propanoic acid}. \]
\[ \Delta H = -0.06936 \ h \]

It is expected the L-2-amino 3-disulfanyl propanoic acid would be present as the zwitterion disulfide anion for this reaction, where the state does not greatly affect the enthalpy change.
The activation energy to open the ring is calculated as, 0.029 h, whilst that to establish the ring is 0.060 h.
The L-2-amino 3-disulfanyl propanoic acid anion may also be formed by the reaction of cysteine anion with elemental sulfur, as,

\[
\begin{align*}
\text{S} & \quad \text{COOH} \\
\text{CH}_2 & \quad \text{NH}_2 \quad \text{CH} \quad \text{COOH} \\
\text{NH}_2 & \quad \text{CH} \quad \text{COOH}
\end{align*}
\]

\[ \Delta H = -0.15542 \ h \]

3.14 The formation of Mg.1,N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin-1-yl.porphin.
The Mg.1,1-amino-2-(2-amino 3-carboxy 1-disulfanyl) ethan-1-yl.porphin readily reacts with any protons to form Mg.1,N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin-1-yl.

\[
\begin{align*}
\text{Mg.1,1-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl.porphin} & \quad + \quad \text{H}^+ \\
& \quad \rightarrow \\
\text{Mg.1,N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin-1-yl.porphin} & \quad + \quad \text{H}_2 + \\
\text{S-S-CH}_2\text{CH(NH}_2\text{)COOH} & \quad \text{H} & \quad \text{H} \\
\text{CH} & \quad \text{NH} \quad \text{N} & \quad \text{H}
\end{align*}
\]

\[ \Delta H = -0.15542 \ h \]

3.15 The formation of the 2-amino 3-carboxypropan 1-disulfanyl ethanimine.
The final dissociation of the Mg.1,N-2-(2-amino 3-carboxy 1-disulfanyl) ethanimin-1-yl.porphin would require heat.

\[
\begin{align*}
\text{Mg.1,2-(2-amino 1-carboxy 3-disulfanyl) ethanimin-1-yl.porphin} & \quad \rightarrow \\
\text{Mg.porphin} & \quad + \quad 2\text{-amino 3-carboxypropan 1-disulfanyl ethanimine}.
\end{align*}
\]

The enthalpy change is,

\[ \Delta H = 0.03825 \ h \]

This is the imine precursor to the amino acid L-cystine.

3.16 The formation of the Mg.1,N-2-amino 3-carboxypropan 1-disulfanyl ethanimine.porphin.CO
The Mg.1,N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin-1-yl.porphin should react with excited carbon monoxide to form an aziridin-2-one complex [12], which has been selected by the excitation of the Mg.porphin.CO complex.[12 ], as shown,

\[
\begin{align*}
\text{Mg.porphin} & \quad + \quad \text{CO} \quad \rightarrow \quad \text{Mg.porphin.CO} \\
\text{Mg.porphin.CO} & \quad + \quad 2\text{-amino 3-carboxypropan 1-disulfanyl ethanimine} \quad \rightarrow \\
& \quad \text{S-S-CH}_2\text{CH(NH}_2\text{)COOH} \\
& \quad \text{H} & \quad \text{H} \\
\text{CH} & \quad \text{NH} \quad \text{N} & \quad \text{H}
\end{align*}
\]

\[ \Delta H = -0.19135 \ h \]
3.17 The Formation of Mg.1,N-2-(2-amino-3-carboxypropan-1-disulfanyl methanyl) aziridine-3-one-1-yl.porphin.

The Mg.1,N-2-amino 3-carboxypropan 1-disulfanyl ethanimine.porphin.CO may easily rearrange to form Mg.1,N-2-(2-amino-3-carboxypropan-1-disulfanyl methanyl) aziridine-3-one-1-yl.porphin., with an activation energy of 0.129 h and a ring dissociation energy of 0.133 h.

\[
\text{Mg.1,N-2-amino 3-carboxypropan 1-disulfanyl ethanimine.porphin.CO} \rightarrow \text{Mg.1,N-2-(2-amino-3-carboxypropan-1-disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin.} \quad [24]
\]

\[
\Delta H = -0.02758 \text{ h}
\]

Such a complex has been inferred as able to polymerise to protein.

3.18 The Formation L-cystine

Hydrolysis in the environment of the complex, is here depicted as releasing the undissociated acid, Fig.3, from the catalyst. Further formation of the zwitterion may occur.

\[
\text{Mg.1,N-2-(2-amino-3-carboxypropan-1-disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin.} \quad [25]
\]

\[
\Delta H = -0.03004 \text{ h}
\]

4. Conclusion

The mechanism described here involving a surface catalysed addition of ammonia to alkynes appears possible according to the laws of thermodynamics and kinetics. However, it still seems apparent that a variety of products will be produced. Hydrolysis of the bifunctional di-aziridin-2-one derivatives should give the protein poly-L-cystine. However, in a mixture of the amino acid precursor aziridine-2-one derivatives, a cross-linked matrix should result (a globular protein) possibly formed in a thermodynamically stable state. The partial or complete severance of the \(-\text{S}--\text{S}-\) bridges would cause some denaturation from the increase in entropy of the molecule, but not necessarily complete destruction of the secondary structure or conformation. This appears to be often found in particular cases [24-25]. Further work at a higher accuracy may alter the values given here.

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