A Prebiotic Surface Catalysed Photochemically Activated Synthesis of L-Cystine

Nigel Aylward
School of Chemistry and Molecular Biosciences
University of Queensland,
Brisbane, Queensland, Australia
uqnaylwa@uq.edu.au

Abstract: - Alkynes such as ethyne form weak charge-transfer, η^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-2one 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-2one 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], is a non-essential amino acid [1] with pK_as 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

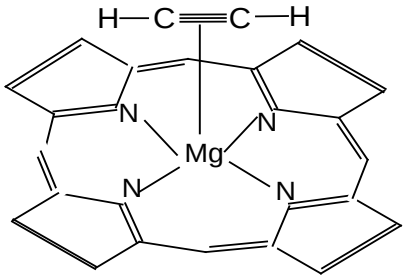
The computations tabulated in this paper used the GAUSSIAN98 [15] commercial package. The standard calculations at the HF and MP2 levels including zero-point energy corrections [16], together with scaling [17], using the same basis set, 6-31G*. are as previously published [7]. Enthalpy changes at the 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].
1h = 627.5095 kcal.mol^{-1}.
1h = 4.3597482 x 10^{-18} J

3 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.

Mg.porphin + H-C≡C-H → Mg.1,ethynyl .porphin
(1) (2) [1]



Mg.1,ethynyl .porphin (2)

Δ H = -0.01807 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
MP2 /6-31G* total energies and zero point energies (hartrees) for the respective equilibrium geometries

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)	-1439.62225	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
S (11)	-397.48197	
S^{--} (12)	-397.33440	
$S\text{-}S^{--}$ (13)	-795.07764	0.00099
Mg.1,1-amino-2-disulfanyl ethan-1-yl.porphin^{--}. (14)	-2113.81879	0.36255
Mg.1,N-2-disulfanyl ethanimin-1-yl. porphin$^-$. (15)	-2113.36441	0.36049
2-disulfanyl ethanimine$^-$ (16)	-928.19404	0.06629
Mg.porphin.CO (17)	-1297.93784	0.30434
Mg.1,N-2-disulfanyl ethanimine.porphin.CO$^-$ (18)	-2226.33676	0.36382
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_2O	-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,

$H\text{-}C{\equiv}C\text{-}H + NH_3 + S\text{-}S^{--} + CO + H_2O + H^+ \rightarrow H_2 + C_3H_6NO_2S_2^-$
L-2-amino 3-disulfanyl propanoic acid$^-$ (3) [2]

Δ H = -0.876293 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,

$H\text{-}C{\equiv}CH + NH_3 + C_3H_6NO_2S_2^- + CO + H_2O + H^+ \rightarrow H_2 + C_6H_{12}N_2O_4S_2$
(3) cystine (4) [3]

Δ H = -0.635941 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],

$$H\text{-}C{\equiv}CH + NH_3 \rightarrow CH_3\text{-}CH{=}NH$$
(5) [4]
$$\Delta H = -0.05767 \text{ h}$$

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

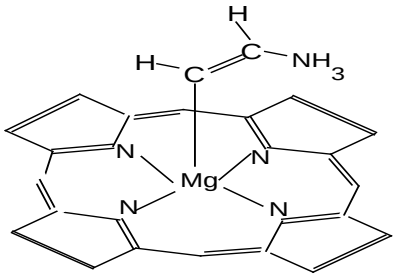
$$CH_2{=}CH\text{-}NH_2 \rightarrow CH_3\text{-}CH{=}NH$$
(6) [5]
$$\Delta H_{(MP2)} = -0.02269. \text{ h}$$

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,

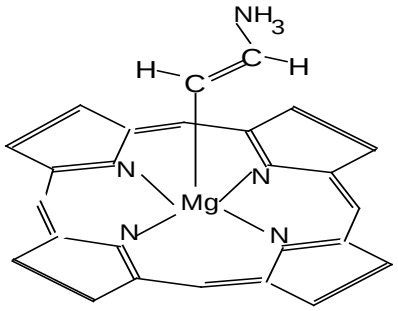
Mg.1,ethynyl.porphin + NH_3 →
cis Mg.1,2-amino ethenyl.porphin
(2) (7) [6]



cis Mg.1,2-amino ethenyl.porphin (7)

$$\Delta H = 0.02676 \text{ h}$$

Mg.ethynyl.porphin + NH_3 →
trans Mg.1,2-amino ethenyl.porphin
(2) (8) [7]



trans Mg.1,2-amino ethenyl.porphin (8)

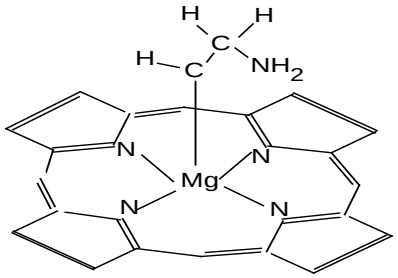
$$\Delta H = 0.04471 \text{ h}$$

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.

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.

cis Mg.1,2-amino ethenyl.porphin →
Mg.1,2-amino ethylidene. porphin.
(7) (9) [8]



Mg.1,2-amino ethylidene.porphin.(9)

$$\Delta H = 0.04375 \text{ h}$$

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

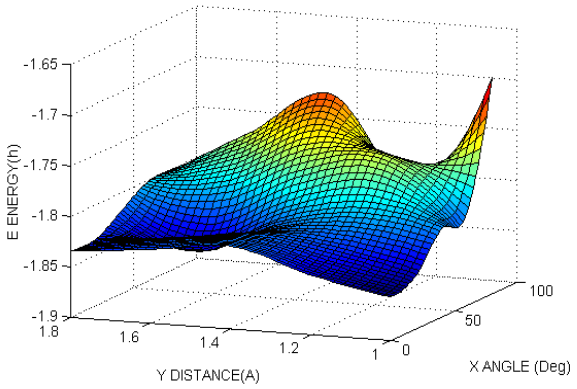


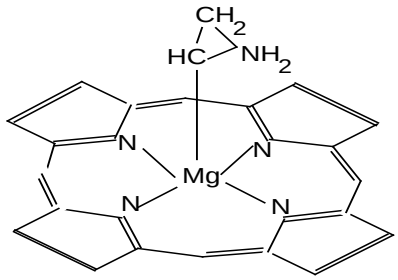
Fig.1. The potential energy surface for the prototropic shift on molecule, cis Mg.1,2-amino ethenyl.porphin. The X-axis depicts the bending of the angle (110.0 - A) degrees, where A is the angle H-N-C(2). The Y-ordinate represents the stretching of the single H-N bond. The minimum for the cis Mg.1,2-amino ethenyl.porphin is at, X=0.0 degrees, Y=1.0 A. A saddle point is at are 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.

cis Mg.1,2-amino ethenyl.porphin →
Mg.1,1H aziridin-2-yl. porphin.
(7) (10) [9]



Mg.1,1H aziridin-2-yl. porphin.
(10)

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

$$\Delta H = -0.00374 \text{ h}$$

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

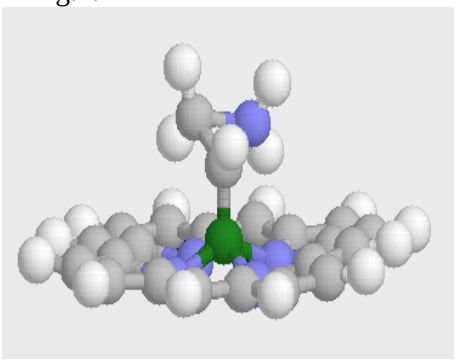


Fig.2. An optimised model of the structure Mg.1,1H- aziridin-2-yl. porphin. (10)

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,

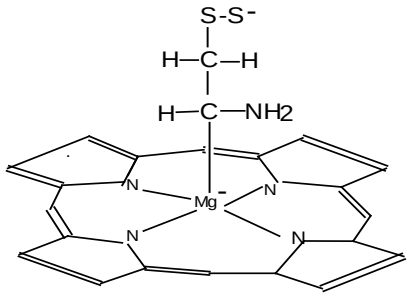
$$S + S^{--} \rightarrow S\text{-}S^{--}$$
(11) (12) (13) [10]

$$\Delta H = -0.26040 \text{ h}$$

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

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

Mg.1,1H aziridin-2-yl. porphin + S-S^{--} →



Mg.1, 1-amino-2-disulfanyl ethan-1-yl. porphin^{--}. (14) [11]

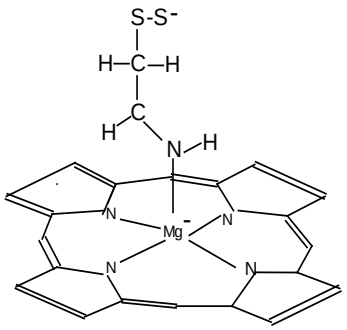
$$\Delta H = -0.19569 \text{ h}$$

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^{-} .

Mg.1,1-amino-2-disulfanyl ethan-1-yl. porphin^{--} + H^+ → H_2 +



Mg.1, N-2-disulfanyl ethanimin-1-yl. porphin^{-}. (15) [12]

$$\Delta H = -0.68218 \text{ h}$$

As the nitrogen of the 3-disulfanyl ethanimine ligand carries a formal negative charge compared to the charge on carbon-1 of the ligand it does isomerise to the more stable charge transfer adduct.

3.9 The formation of the 2-disulfanyl ethanimine^{-}.

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

Mg.1,N-2-disulfanyl ethanimin-1yl. porphin^{-} → Mg.porphin + 2-disulfanyl ethanimine^{-} (16) [13]

The enthalpy change is,

$$\Delta H = 0.04647 \text{ h}$$

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

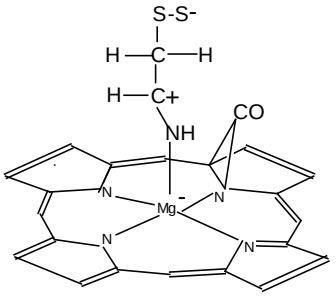
3.10 The formation of the Mg.1,N-2-disulfanyl ethanimin-1yl .porphin.CO^{-}

The Mg.1,N-2-disulfanyl ethanimin-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,

Mg.porphin + CO → Mg.porphin.CO (1) (17) [14]

$$\Delta H = 0.21136 \text{ h}$$

Mg.porphin.CO + 2-disulfanyl ethanimine^{-} → (17) (16)



Mg.1,N-2-disulfanyl ethanimin-1yl .porphin.CO^{-} (18) [15]

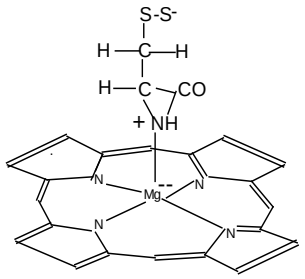
$$\Delta H = -0.21094 \text{ h}$$

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.

Mg.1,N-2-disulfanyl ethanimin-1yl.porphin.CO$^-$ (18) →



Mg.1,N-2-(disulfanyl methanyl) 1H- aziridine-3-one-1-yl.porphin$^-$.(19) [16]

$$\Delta H = -0.02178 \text{ h}$$

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.

Mg.1,N-2-(disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin$^-$ + H_2O → Mg.porphin + L-2-amino-3-disulfanyl propanoic acid$^-$. (3) [17]

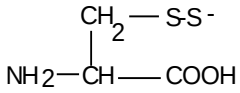


Fig.3. L-2-amino-3-disulfanyl propanoic acid$^-$. (3)

$$\Delta H = -0.02382 \text{ h}$$

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

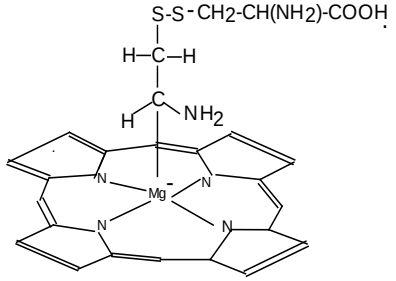
MP2 /6-31G* total energies and zero point energies (hartrees) for the respective equilibrium geometries

Molecule	MP2 hartree	ZPE (HF) hartree
Mg.1,1-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl. porphin$^-$ (20)	-2436.08551	0.47150
(20) zwitterion	-2436.08867	0.47218
cysteine$^-$ non-zwitterion (21)	-719.83045	0.10667
Mg.1, N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin -1-yl.porphin (22)	-2435.51088	0.46315
(22) zwitterion	-2435.50986	0.46325
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 (25)	-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,

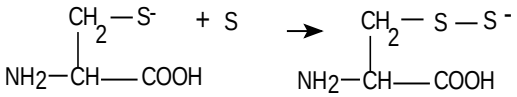
Mg.1,N-1H aziridin-2-yl. porphin + $C_3H_6NO_2S_2^-$ L-2-amino 3-disulfanyl propanoic acid$^-$ → (3)



Mg.1,1-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl. porphin$^-$. (20) [18]

$$\Delta H = -0.06936 \text{ h}$$

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,



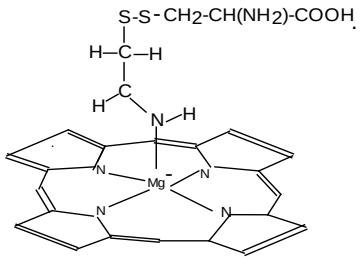
(21) [19]

$$\Delta H = -0.15542 \text{ h}$$

3.14 The formation of Mg.1,N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethenimin-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.

Mg.1, 1-amino-2-(2-amino 3-carboxypropan 1-disulfanyl) ethan-1-yl. porphin$^-$ + H^+ → H_2 +



Mg.1, N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin -1-yl.porphin. (22) [20]

$$\Delta H = -0.56748 \text{ h}$$

As the nitrogen of the 2-amino 3-carboxypropan 1-disulfanyl ethanimine ligand carries a formal negative charge compared to the charge on carbon -1 of the ligand it does isomerise to the more stable charge transfer adduct.

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.

Mg.1, 2-(2-amino 1-carboxy 3-disulfanyl) ethanimin-1-yl.porphin →
Mg.porphin + 2-amino 3-carboxypropan 1-disulfanyl ethanimine. (23) [21]

The enthalpy change is,

$$\Delta H = 0.03825 \text{ h}$$

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

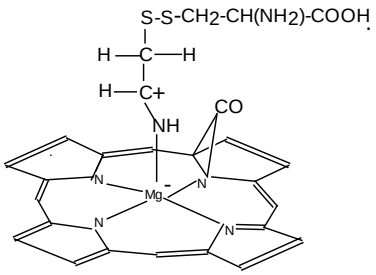
The Mg.1,N-2-(2-amino 3-carboxypropan 1-disulfanyl) ethanimin-1-yl.porphin should react with excited carbon monoxide to form an aziridin-2-one complex [12], which has been selected by the excitation of the Mg.porphin.CO complex.[12], as shown,

Mg.porphin + CO → Mg.porphin.CO
(1) (17) [22]

$$\Delta H = 0.21136 \text{ h}$$

This should be easily dissociable by heat.

Mg.porphin.CO + 2-amino 3-carboxypropan 1-disulfanyl ethanimine (23) →



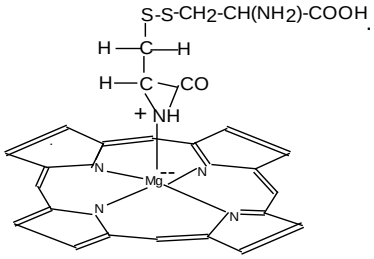
Mg.1,N-2-amino 3-carboxypropan 1-disulfanyl ethanimine.porphin.CO (24) [23]

$$\Delta H = -0.19135 \text{ h}$$

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.

Mg.1,N- 2-amino 3-carboxypropan 1-disulfanyl ethanimine.porphin.CO (24)
→



Mg.1,N-2-(2-amino-3-carboxypropan-1-disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin. (25) [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.

Mg.1,N-2-(2-amino-3-carboxy-1-disulfanyl methanyl) 1H-aziridine-3-one-1-yl.porphin. + H_2O → Mg.porphin + L-cystine (4) [25]

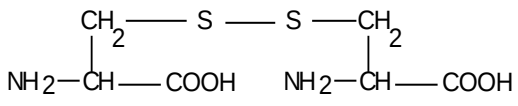


Fig.3. L-cystine (4)

$$\Delta H = -0.03004 \text{ h}$$

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-2one derivatives, a cross-linked matrix should result (a globular protein) possibly formed in a thermodynamically stable state. The partial or complete severance of the –S—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.

5 Acknowledgements

Appreciation is expressed for the advice and support given to this project by Professor Curt Wentrup of the University of Queensland.

Appreciation is also expressed to the National Computing Infrastructure facility supported by the Australian Government (grant NCI-MAS g01) and QCIF, and the assistance of Mr.D.Green, H.Hartig and M.Hankel

References

[1] A.L.Lehninger, *Biochemistry*,Worth, New York ,1975.

[2] R.K.Cannan and B.C.G.Knight, Dissociation constants of cystine, cysteine, thioglycollic acid and α-thiollactic acid, *Biochem.J.*,21, 1927, pp.1384-1390.

[3] R.C.Fahey, J.S.Hunt, G.C. Windham, On the cystine and cysteine content of proteins, *J.Mol.Evol*., 10, No.2,1977, pp.155-160.

[4] J. P. Greenstein, M. Winitz, *Chemistry of the Amino Acids* vols 1-3, John Wiley and Sons, Inc., New York, 1961.

[5] G.N.Ramachandran, *Conformation of biopolymers*, Academic Press, Vol.1,1967.

[6] F.Challenger, *Aspects of the Organic Chemistry of Sulfur*, Butterworths Scientific Publications, 1959.

[7] N.Aylward, and N.R.Bofinger, Possible origin for porphin derivatives in prebiotic chemistry - a computational study, *Orig.Life Evol. Biosph.*,35, No.4, pp345-368,2005.
[8] S.L.Miller and L.E.Orgel, *The Origins of Life on Earth*, Prentice-Hall Inc.,Englewood Cliffs, N.J. ,1975.
[9] D.W.Clarke and J.P.Ferris, Photodissociation of cyanoacetylene : application to the atmospheric chemistry on Titan, *Icarus*, vol.115,1995, pp.119-125.
[10] K.Seki, M.He, R.Liu and H.Okabe, Photochemistry of cyanoacetylene at 193.3 nm., *J.Phys.Chem*.,100 ,1996, pp.5349-5353.
[11] Z.Guennoun, A.Coupeaud, I.Couturier-Tamburelli, N.Pietri, S.Coussan, J.P.Aycard, Acetylene/cyanoacetylene complexes:simulation of the Titan's atmosphere chemistry, *Chem.Phys*.300, 2004, pp.143-151.
[12] N.N.Aylward, and N.R.Bofinger, Carbon monoxide clusters in the formation of D-sugars and L-amino-acids in prebiotic molecular evolution on Earth, in G.Palyi, C.Zucchi, L.Cagliotti, eds., *Progress in Biological Chirality*, Elsevier,Oxford (GB), 2004, ch2, pp.429.
[13] N.N. Aylward, The synthesis of terpenes in prebiotic molecular evolution on Earth, in WSEAS *New Aspects of Biomedical Electronics and Biomedical Informatics*. Eds. C.A.Long, P.Anninos, T.Pham, G.Anastassopoulos, N.E.Mastorakis, 2008, pp.202-207
[14] E T. Parker, H. J. Cleaves, M. P. Callahan, J. P. Dworkin, D. P. Glavin, A. Lazcano, J. L. Bada, Prebiotic synthesis of methionine and other sulfur-containing organic compounds on the primitive Earth: A contemporary reassessment based on an unpublished 1958 Stanley Miller experiment, *OLEB*, 41, No.3, 2011, pp. 201–212.
[15] Gaussian98, *Users Reference,Gaussian* Inc.,Carnegie Office Park, Bldg.6., Pittsburgh, PA 15106, USA,1998.
[16] W.J.Hehre, L.Random, P.V.R. Schleyer, and J.A.Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York.,1986.
[17].J.A.Pople, H.B.Schlegel, R.Krishnan, D.J. DeFrees, J.S. Binkley, M.J. Frisch, R.A.Whiteside, R.J.Hout and W.J.Hehre, Molecular orbital studies of vibrational frequencies, *Int.J.Quantum Chem. Symp*. vol.S15,1981, pp.269-278.
[18] D.G.Whitten,I.G.Lopp and P.D.Wildes, Fluorescence of zinc and magnesium etioporphyrin 1. quenching and wavelength shifts due to complex formation, *J.Am.Chem.Soc*., 90, 1968, pp.7196-7200.
[19] N.N.Aylward, and N.R.Bofinger, The reactions of carbon monoxide with methanimine and cyanogen in prebiotic molecular evolution on Earth, *Orig. Life Evol. Biosph*, vol.6, 2001, pp.481-500. 1
[20] N. Aylward, A prebiotic surface catalysed synthesis of alkyl imines,in WSEAS Int. Conf. on *Biomedical Electronics and Biomedical Informatics*. Moscow, Russia, August 20-22, 2009, pp.52-59.
[21] N.Aylward, A prebiotic surface catalysed synthesis of alkyl imine precursors to the amino acids, alanine, serine and threonine, WSEAS *Transactions on Biology and Medicine*, 6, No.2 ,2009, pp.27-37.
[22] N.N.Aylward, A prebiotic surface catalysed photochemically activated synthesis of L-cysteine, *Adv.Biol.Sci.Res*.,3, 2017, pp.1-5.
[23] T.Moeller, *Inorganic Chemistry*, J.Wiley, 1952.
[24] E.Drakopoulon, J.Vizzavona, J.Neyton, V.Aniort, F.Bouet, H.Virelizier, A.Menez, C.Vita, Cosequence of the removal of evolutionary conserved disulphide bridges on the structure and function of charybdotoxin, *Biochemistry*, 37,No.5, 1998, pp.1292-1301.
[25] L.Moroder, H.J. Musiol, M.Goty, C.Reuner, Synthesis of single- and multiple- stranded cysteine-rich peptides, *Biopolymers*, 40, No.2, 1996, pp.207-234.