A Prebiotic Surface Catalysed Photochemically Activated Synthesis of L-Methionine and L-Homocysteine

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

Abstract: - Alkynes such as propyne nitrile and propynimine 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 changes are -0.024 and -0.040 h, respectively. Addition of methyl thiol to the complexes allows the formation of Mg.1,N-3-methylsulfanyl propenyl nitril-1yl.porphin and Mg.1,N-3-methylsulfanyl propenylimin-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 and reducible to the amino acid L-methionine. With hydrogen sulphide addition an analogous set of reactions yields L-homocysteine.
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: propyne nitrile, propynimine, 2-(2-methylsulfanyl ethenyl) aziridine 3-one, Mg.porphin, L-methionine, homocysteine.

1 Introduction

L-methionine, (2S)-2-amino-4-(methylsulfanyl) butanoic acid, α-amino-γ-methylmercapto butyric acid, S-methyl homocysteine, [1], Met, M, is an essential amino acid with pK_aCOOH 2.28, pK_aNH_3 9.21 [2]. The configuration has been established as L-methionine [3]. In its synthesis by the Strecker method methane thiol is added to acrolein [4]. The direction of the addition of the methane thiol may be determined by the polarisation of the conjugated system [5]. It accounts for 2-4% of the protein in sulfur containing proteins [6] It is converted in the body to cysteine in which serine is involved and it is closely involved with the phenomenon of biological methylation [7]. The degradation of methionine to homocysteine is described [1] and its biosynthesis from homocysteine [1].
From a prebiotic perspective [8] 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 [1,9] implying the presence of concentrations of carbon monoxide, ammonia, water, hydrogen and hydrogen sulfide. It is also supposed that alkynes such as acetylene [10-11] were present as found on Titan, a moon of Saturn [12]. It has also been demonstrated that porphin may act as a catalyst for the formation of sugars [13] and polyenes [14].
This paper proposes a model for the catalytic photochemically activated formation of L-methionine from the gases, cyanoacetylene, carbon monoxide, hydrogen, methyl mercaptan, water and the catalyst magnesium porphin. An experimental gaseous mixture subjected to discharge has also produced the amino acid methionine [15].

2 Problem Formulation

The computations tabulated in this paper used the GAUSSIAN98 [16] commercial package. The standard calculations at the HF and MP2 levels including zero-point energy corrections [17], together with scaling [18], using the same basis set, 6-31G*. are as previously published [8]. 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 [17].
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 [16].
1h = 627.5095 $kcal.mol^{-1}$.

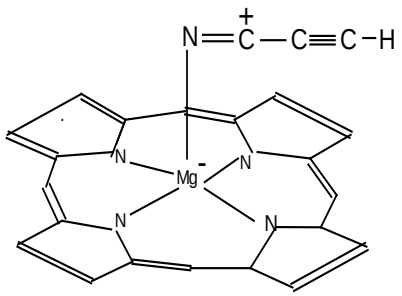
1h = 4.3597482 x 10^{-18} J

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 [19]. With cyanoacetylene the ligand is positively charged (0.07) and the porphin has a negative charge. The cyanoacetylene sets as ligand with a linear N≡C-C≡C-H structure as shown [20-22].

Mg.porphin + N≡C-C≡C-H → Mg.1,N-propyne nitril-1yl.porphin
(1) (2) (3) [1]



Mg.1,N-propyne nitril-1yl.porphin
(2)

Δ H = -0.02385 h

The propyne nitrile may be reduced in the atmosphere to propynimine,

N≡C-C≡C-H + H_2 → HN=CH-C≡C-H
(2) (4) [2]
Δ H = -0.00021 h

A similar charge transfer complex is formed with propynimine,

Mg.porphin + HN=CH-C≡C-H → Mg.1,N-propynimin-1yl.porphin
(1) (4) (5) [3]

Δ H = -0.03965 h

The data for the total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for.these molecules 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
propyne nitrile (2)	-169.0791	0.02976
Mg.1,N-propyne nitril-1yl.porphin (3)	-1354.22133	0.31789
propynimine(4)	-170.23556	0.05408
Mg.1,N-propynimin-1yl.porphin (5)	-1355.39431	0.34290
L-methionine(6)	-798.71994	0.17946
methyl mercaptan(7)	-437.95267	0.04942
Mg.1,N-3-methyl sulfanyl 2-propenyl nitril-1yl.porphin (8)	-1792.24706	0.37399
Mg.1,N-3-methylsulfanyl propenylimin-1yl.porphin (9)	-1793.42036	0.39974
3-methyl sulfanyl 2-propenimine(10)	–608.25578	0.11163
Mg.porphin.CO(11)	-1297.93784	0.30434
Mg.1,N-3-methyl sulfanyl 2-propenimin-1yl.porphin.CO (12)	-1906.40292	0.40961
Mg.1,N-2-(2-methyl sulfanyl ethenyl) 1H-aziridine-3-one-1-yl.porphin (13)	-1906.40982	0.40980
Mg.1,N-3-sulfanyl propenylimin-1yl.porphin (14)	-1754.25145	0.36836
L-homocysteine (15)	-759.56049	0.14820
CO	-113.02818	0.00484
H_2S	-398.78841	0.01645
CH_2=S	-436.75511	0.02389
CH_4	-40.33255	0.04778
H_2	-1.14414	0.01034
OH^-	-75.51314	0.00885
H_2O	-76.19924	0.02148

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

Although Mg.porphin is here taken as the catalyst for the reaction, the overall stoichiometry for the synthesis of methionine from cyanoacetylene, methyl mercaptan, carbon monoxide, water and hydrogen can be represented as follows,

N≡C-C≡CH + CH_3-SH + CO + H_2O + 2H_2 → $C_5H_{11}NO_2S$ L-methionine (6) [4]

$\Delta H = -0.13693$ h

The enthalpy change is negative indicating that there may be energetically favourable routes to the formation of this amino acid.
The methyl mercaptan is expected to have arisen from the reaction of gaseous methane and hydrogen sulfide, or the reduction of thioformaldehyde [23],

$CH_4 + H_2S \rightarrow CH_3\text{-}SH + H_2$ [5]
(7)
$\Delta H = 0.02041$ h

$CH_2{=}S + H_2 \rightarrow CH_3\text{-}SH$ [6]
(7)
$\Delta H = -0.04012$ h

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

3.3 The formation of the methyl sulfanyl complex.

Methyl mercaptan may react with the Mg.1,N-propyne nitril-1yl.porphin and Mg.1,N-propyn imin-1yl.porphin in addition reactions where the orientation is determined by the bond polarization [5], Fig.1.

Mg.1,N-propyne nitril-1yl.porphin + $CH_3SH \rightarrow$
(3) (7)

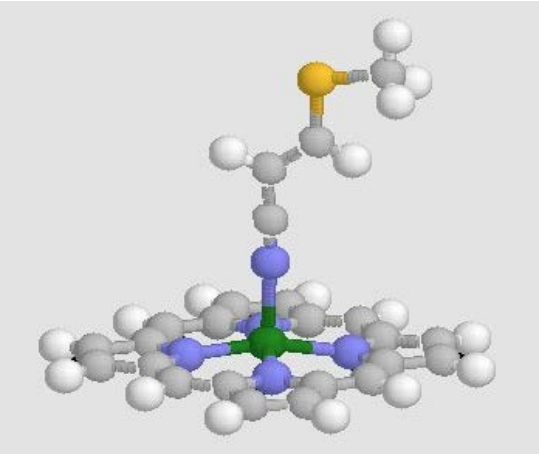


Fig.1. Mg.1,N-3-methyl sulfanyl 2-propenyl nitril-1yl.porphin (8) [7]
$\Delta H = -0.06737$ h

The corresponding reaction with the Mg.1,N-propynimin-1yl.porphin is:

Mg.1,N-propynimin-1yl.porphin + $CH_3SH \rightarrow$
(5) (7)
Mg.1,N-3-methylsulfanyl propenylimin-1yl.porphin
(9) [8]

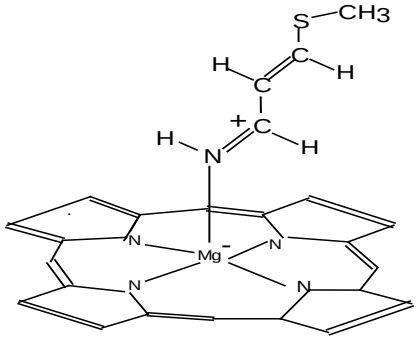
$\Delta H = -0.06677$ h

The activation energy for the formation of the methyl mercaptan adduct with a transfer mechanism was 0.095 h whilst the reverse reaction had an activation energy of 0.159 h.

3.4 The hydrogenation of Mg.1,N-3-methyl sulfanyl 2-propenyl nitril-1yl.porphin

Under the presumed mildly reducing atmosphere the addition of hydrogen should occur in a favourable addition reaction, as follows:

Mg.1,N-3-methyl sulfanyl 2-propenyl nitril-1yl. porphin + $H_2 \rightarrow$
(8)



Mg.1,N-3-methylsulfanyl 2-propenylimin-1yl.porphin (9) [9]

$\Delta H = -0.01566$ h

3.5 The formation of the 3-methyl sulfanyl 2-propenimine.

The Mg.1,N-3-methylsulfanyl 2-propenylimin-1yl.porphin may dissociate the 3-methyl sulfanyl 2-propenimine with a realisable vapour pressure,

Mg.1,N-3-methylsulfanyl 2-propenylimin-1yl.porphin (9) $\rightarrow$
Mg.porphin + 3-methyl sulfanyl 2-propenimine
(10) [10]

$\Delta H = 0.04610$ h

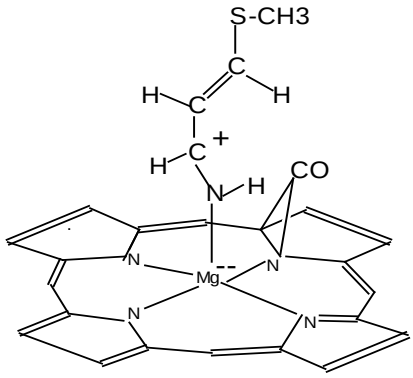
This is the imine precursor to the amino acid methionine.

3.6. The formation of Mg.1,N-3-sulfanyl propenimin-1yl.porphin.CO

Imines have been previously shown to react with excited carbon monoxide to form aziridin-2-one complexes [13,20-22] which should be easily dissociable by heat and hydrolysable.
For the correct formation of the L-isomer the 3-methylsulfanyl 2-propenimine needs to chelate to the magnesium ion on a Mg.porphin which has already obtained the correct orientation of a bound carbon monoxide molecule [13], as shown.

Mg.porphin.CO + 3-methyl sulfanyl 2-propenimine

(11) (10)



Mg.1,N-3-methyl sulfanyl 2-propenimin-1yl.porphin.CO (12) [11]

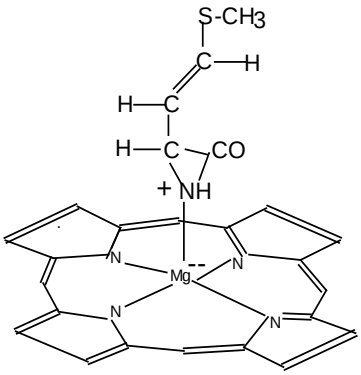
$$\Delta H = -0.21496 \text{ h}$$

The enthalpy change is favourable and the activation energy to form van der Waals complexes is usually not significant if they are spontaneous.

3.7. The formation of Mg.1,N-2-(2-methyl sulfanyl ethenyl) 1-H aziridine-3-one-1-yl.porphin

The Mg.1,N-3-methyl sulfanyl 2-propenimin-1yl.porphin.CO may easily rearrange to form Mg.1,N-2-(2-methyl sulfanyl ethenyl) 1-H aziridine-3-one-1-yl.porphin with an activation energy of 0.144 h and a ring dissociation energy of 0.133 h.

Mg.1,N-3-methyl sulfanyl 2-propenimin-1yl.porphin.CO (12) →



Mg.1,N-2-(2-methyl sulfanyl ethenyl) 1-H aziridine-3-one-1-yl.porphin (13) [12]

The enthalpy change is favourable.

$$\Delta H = -0.0067 \text{ h}$$

3.8. The formation L-methionine.

Hydrolysis in the environment of the complex, is here depicted as releasing the undissociated acid, Fig.2, from the catalyst. Further formation of the zwitterion may occur.

Mg.1,N-2-(2-methyl sulfanyl ethenyl) 1-H aziridine-3-one-1-yl.porphin + $H_2O + H_2$ → Mg.porphin + L-methionine (6) [13]

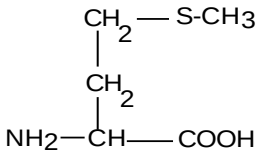


Fig.2. L-methionine (6)

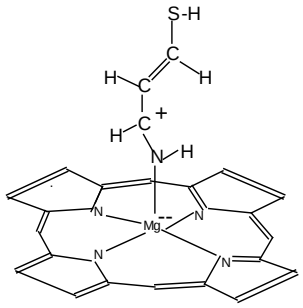
$$\Delta H = -0.06607 \text{ h}$$

3.9 The Formation of the homocysteine complex.

Similar to the addition of methyl mercaptan, hydrogen sulfide gas may react with the Mg.1,N-propynimin-1yl.porphin in an addition reaction

where the orientation is determined by the bond polarization [5], as shown,

Mg.1,N-propynimin-1yl.porphin + H_2S →
(5)



Mg.1,N-3-sulfanyl propenylimin-1yl.porphin
(14) [14]

$\Delta H = -0.03489$ h

The activation energy for the formation of the hydrogen sulfide adduct with a transfer mechanism was 0.106 h whilst the reverse reaction had an activation energy of 0.135 h.

Exactly similar reactions to those for Mg.1,N-3-methyl sulfanyl 2-propenimin-1yl.porphin, should yield the amino acid L-homocysteine.

$N\equiv C\text{-}C\equiv CH + H_2S + CO + H_2O + 2H_2 \rightarrow C_4H_9NO_2S$ L-homocysteine (15) [15]

$\Delta H = -0.14022$ h

4. Conclusion

The imine, propynimine, should be readily available in prebiotic chemistry from the partial reduction of cyanoacetylene, found in electrical discharge of an atmosphere containing hydrocarbon and nitrogen [9] and the interstellar medium. Similarly, methyl mercaptan should be readily available from free radical or ionic reactions containing some methane and hydrogen sulphide. These reactants do appear to offer at least one mechanism to the formation of the essential amino acid, L-methionine, according to thermodynamic and kinetic considerations as depicted here.

Apart from cyanoacetylene forming a charge complex with Mg.porphin through bonding to the nitrogen atom, it may also bond to the methine carbon of cyanoacetylene [24]. Analogous reactions as depicted here then yielding ultimately the rare amino acid, β-cyanoalanine [1]. Exactly similar bonding and reactions using propynamine would yield ultimately the rare amino acid, β-alanine [1]. Both of which have some presence today.

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] D.Voet and J.Voet, *Biochemistry*, J.Wiley, 2011.

[3] E.E.Conn and P.K.Stumpf, *Outlines of Biochemistry*, John Wiley Inc.1972, pp.528.

[4] E.E.Turner and M.M.Harris, *Organic Chemistry*, Longmans, 1952, pp.202.

[5] C.K.Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell Univ. Press. 1953, pp.649.

[6] K.Bailey, Proteins, in Rodd,E.H.(ed), *Chemistry of Carbon Compounds*, Elsevier, Amsterdam, Vol.1B, 1952.

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

[8] N.Aylward, and N.R.Bofinger, Possible origin for porphin derivatives in prebiotic chemistry - a computational study, *Orig.Life Evol. Biosph.*, 35, No.4, 2005, pp.345-368.

[9] S.L.Miller and L.E.Orgel, *The Origins of Life on Earth*, Prentice-Hall Inc.,Englewood Cliffs, N.J., 1975.

[10] D.W.Clarke and J.P.Ferris, Photodissociation of cyanoacetylene : application to the atmospheric chemistry on Titan, *Icarus*, vol.115, 1995, pp.119-125.

[11] K.Seki, M.He, R.Liu and H.Okabe, Photochemistry of cyanoacetylene at 193.3 nm., *J.Phys.Chem*.,100 ,1996, pp.5349-5353.

[12] 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.
[13] 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.
[14] 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
[15] 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.
[16] Gaussian98, *Users Reference*,Gaussian Inc.,Carnegie Office Park, Bldg.6., Pittsburgh, PA 15106, USA, 1998.
[17] W.J.Hehre, L.Random, P.V.R. Schleyer, and J.A.Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York.,1986.
[18] 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.
[19] 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.
[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*, 6,2, 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] N.N.Aylward and N.R.Bofinger, An ab initio computational study of thiamin synthesis from gaseous reactants of the interstellar medium. *Biophysical Chemistry* 121, No.3, 2006, pp.185-193.
[24] N.N.Aylward, A computational study of a prebiotic synthesis of L-asparagine and L-aspartic acid, 6 th. WSEAS Congress: *Applied Computing Conference 2013* (ACC 13),Nanjing, China, November 17-19, 2013.