

A Computational Study of a Prebiotic Synthesis of L-Leucine, L-Isoleucine and L-Proline

N. AYLWARD

Queensland University of Technology,
George Street,
Brisbane,
AUSTRALIA
n.aylward@alumni.qut.edu.au

Abstract: - The magnesium ion metalloporphyrin complex is shown to bind the ligands pent-1,3-diyne and but-1,3-diyne in weak van der Waals complexes on the metal site and act as a photochemical catalyst. Subsequent reaction of the adducts with ammonia gives amines that easily transform to aziridine derivatives, and ultimately imines bound to the catalyst. When carbon monoxide is also bound to the complex as a high energy compound whose particular structure has been dictated by the magnetic vector of the exciting radiation, reaction occurs to give substituted aziridine-2-ones that may easily hydrolyse to the zwitterionic form of the amino acids L-leucine, L-isoleucine, and L-proline.

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, and with acceptable activation energies

Key-Words: - Prebiotic photochemical synthesis, L-leucine, L-isoleucine, L-proline.

1 Introduction

The amino acids L-leucine (Leu,L) and L-isoleucine (Ile,I), are essential amino acids [1], that occur naturally as the L-isomer [2] and are present in many proteins such as haemoglobin, elastin, wool keratin, myosin and ovalbumin [2]. N-Methylleucine occurs naturally in seeds of *Cycas circinalis* and *Phaseolus vulgaris*[3]. Norleucine, α -aminocaproic acid also has a natural occurrence in an ergot alkaloid [4]. L-proline (Pro) [1], pyrrolidine-2-carboxylic acid, is a non-essential amino acid present in prolamines such as gliadin in wheat and zein from maize [2], and protein fibres such as elastin [2], collagen [5-7], and gelatin [8].

Isoleucine contains two asymmetric carbon atoms and therefore exists in two racemic forms, DL-isoleucine and DL-alloisoleucine giving four optical isomers. The configuration of normal L-isoleucine is 2S, 3S [1]. L-proline is a cyclic amino acid which has been configurationally related to L-arginine [2]. The α -carbon is R. These amino acids are hydrophobic [9] and normally present in solution as zwitterions. L-leucine has α -COOH pKa, 2.36 and an α -NH₂ pKa 9.60 [1], for isoleucine the corresponding values are 2.4 and 9.7 [10], and for L-proline the carboxyl pKa is at 1.95, and the amino pKa at 10.64 [11] with an isoelectric point of 6.3

The biosynthesis of leucine is from α -ketovaleric acid [1] and isoleucine from α -ketobutyric acid [1].

The metabolism of L-leucine yields acetyl-CoA in the tricarboxylate cycle [1]. The metabolism of isoleucine leads to succinyl-CoA [1]. The biosynthesis of L-proline has been described [1], in which all five carbon atoms arise from glutamic acid, where the amino group has been formed directly from ammonia and α -ketoglutarate, whilst in the catabolism of L-proline glutamic acid is formed. 4-hydroxyproline is formed subsequently from preformed L-proline residues [1]. The codons for proline are CCU, CCG, CCC and CCA [1].

From a prebiotic perspective [12] 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 [1,13] implying the presence of concentrations of carbon monoxide, ammonia, water and hydrogen. It is also supposed that alkynes such as methyl diacetylene, $CH_3 - (C \equiv C)_2 - H$, that has been found in interstellar space [14] was also present, possibly formed from the free radical mediated condensation of acetylene and allylene or by ionic species [15], and diacetylene found to be present on Titan, a moon of Saturn [16]. The gas diacetylene has been proposed as a prebiotic source of the amino acids histidine [17], arginine [18], lysine [19], phenylalanine [20] and tryptophan [21]. It has also

been demonstrated that porphin may act as a catalyst for the formation of sugars [22], polyenes [23].

This paper proposes a model for the catalytic photochemically activated formation of L-leucine, L-isoleucine and L-proline from methyl diacetylene, diacetylene, ammonia, carbon monoxide, hydrogen, and the catalyst magnesium porphin, whilst seeking to explain the meager occurrence of norleucine and ψ -leucine [2]. The chemistry of carbon monoxide encompasses a number of carbonylation reactions [24] in which it becomes bonded as a ligand to a transition metal complex, M-R, that also contains another ligand, R [25]. The "migratory insertion" reaction forms a compound M-CO-R [26]. With suitable ligands, R, the reactions comprise, hydroformylation giving aldehyde, R-CH=O molecules, reductive carbonylation [27] giving isocyanate, R-N=C=O, carbamates, R-NH-CO-OR, ureas R-NH-CO-NR, and amines R-NH₂, β -lactams [28] and carbon-nitrogen bonds [29]. However, the metalloporphin catalyst used in this study only allows axial substituents, restricting the above reactions which require a cis orientation of CO and the ligand, R [30].

The reaction proposed here requires a nucleophilic or electrophilic attack of a carbon monoxide molecule immobilised, and specifically oriented and energised with photochemical energy of (0.20 h) to react with the imine in an asymmetric synthesis [22]. The equilibration reaction involves the carbon monoxide transferring from being bonded to a C=N bond as an aziridine-2one centered on a peripheral pyrrole unit to being bonded to a C=N bond on the adduct as an aziridine-2one. The potential energy surfaces for ground state reactions of carbon monoxide with gas phase alkyne [31] and imine [22,31] together with the marginally unfavourable enthalpy changes and activation energies are more attainable if the alkyne or imine are bonded as charge-transfer complexes on the catalyst Mg.porphin which can absorb appreciable electromagnetic radiation. The enthalpy changes may become marginally favourable [32] and the activation energies easily attainable [21].

The reactions described have been deduced as kinetically and thermodynamically viable, but photochemical excitation is required.

2 Problem Formulation

This proposed computational study of plausible syntheses of L-leucine, L-isoleucine and L-proline involves the calculation of the enthalpy changes for reaction intermediates in the ZKE approximation

and the calculation of activation energies at the HF level. These activation energies may all be accessible as the catalyst may absorb appreciable photochemical activation (0.21 h). The computations tabulated in this paper used the GAUSSIAN03 [33] commercial package. The standard calculations at the HF and MP2 levels including zero-point energy corrections at the Hartree Fock level, [34], together with scaling [35], using the same basis set, 6-31G*. are as previously published [12]. 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 [34], and activation energies calculated at the HF level without scaling are less accurate.

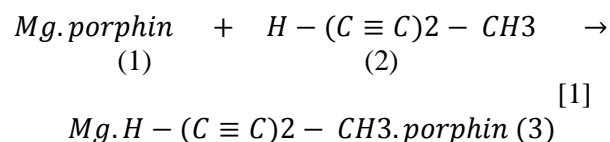
If the combined energy of the products is less than the combined energy of the reactants it may show that the reaction is also likely to be spontaneous at higher temperatures. This paper uses the atomic unit of energy, the hartree [33].

1h = 627.5095 kcal.mol⁻¹. 1h = 4.3597482 x 10⁻¹⁸ J
Charges are in units of the electronic charge.

3 Problem Solution

3.1 Total Energies (hartrees)

Methyl diacetylene may chelate with the magnesium ion of magnesium porphin, which is here taken as a possible catalyst, to form an in-plane charge transfer complex where the charge on the ligand is positive, 0.06. and the charge on the porphin molecule is negative. The enthalpy of formation of the van der Waals complex is small but it appears stable.

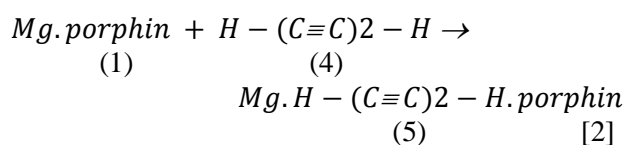


$$\Delta H = -0.02556 h$$

The adduct has formal charges of -0.59, 0.22, 0.19, -0.23 and -0.50 on the carbons C1-C4, respectfully. This is the first reactant required in the synthesis of L-leucine and L-isoleucine.

Similarly, diacetylene may chelate with the magnesium ion of magnesium porphin, to form an in-plane charge transfer complex where the charge

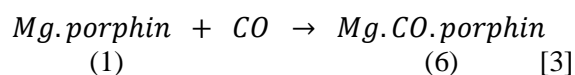
on the ligand is positive, 0.08. and the charge on the porphin molecule is negative. The enthalpy of formation of the van der Waals complex is small but it appears stable.



$$\Delta H = -0.01480 h$$

3.2 The asymmetric induction of chirality

Mg.porphin also forms a stable complex with carbon monoxide in which the carbon monoxide is bonded to the magnesium ion, as shown,



$$\Delta H(\text{HF}) = -0.00919 h$$

This is the low energy complex [22]. When this complex is photochemically activated, an in-plane electronic transition occurs in which the HOMO may be excited to the LUMO [22]. If the magnetic vector of the radiation is directed perpendicularly upward from the ring when viewed from above, the energy levels of the HOMO and LUMO are each split according to the Zeeman effect [36] and the adduct may dissociate, and rise in height above the ring. The first excitation energy (0.21 h) is greater than the activation energy (0.19668 h) and much greater than the bonding energy (-0.02164 h) [22]. The system of conjugated bonds in porphin has been approximated to the particle on a ring quantum mechanical problem [37]. In this model the molecule is described as a cyclic system [38] where the removal of the degeneracy of the orbitals by the magnetic field allows the contributing mesomeric forms [39] to have different energies, as shown in Fig.1.

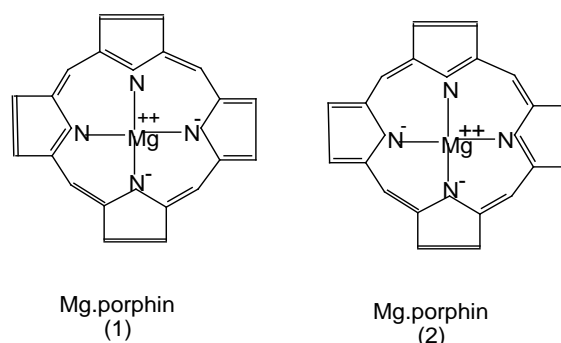


Fig.1. Mesomeric forms of Mg.porphin in the presence of a magnetic field pointing perpendicularly upwards from the ring towards the observer.

Four transitions may occur [36] of which two are allowed by the selection rules [40]. As the molecule is normally diamagnetic [41] the highest energy HOMO orbital should correspond to that shown as Fig.1(1). It is postulated that the CO group is able to move through a transition state to the porphin ring where it forms an excited, but stable bridged aziridine-2-one ring [22,26,42] at a pyrrole unit with this isomer, as shown, Fig.2(1)

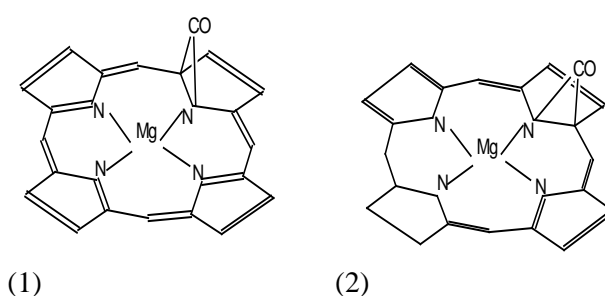
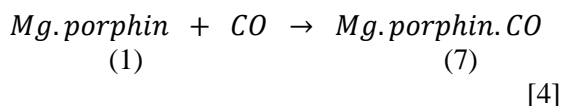


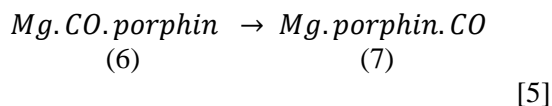
Fig.2. Isomers of Mg.porphin.CO

This is a higher energy charge transfer complex, where a high proportion of the photochemical energy has been conserved as chemical energy. If the magnetic field reverses the positively charged adduct is compressed down on the ring and less liable to reaction. If the unfavourable complex Fig.2(2) is formed from atmospherically activated carbon monoxide, then further excitation may lift the adduct from the periphery of the ring and convert it to the more favourable orientation for asymmetric induction. The activation energy required to convert the forms Fig.2(1) to Fig.2(2) is < 0.11 h.

This is also involved in the proposed synthesis, as shown later. The formation requires photochemical activation. The enthalpy of formation is positive.



$$\Delta H = 0.21136 h$$



$$\Delta H = 0.20106 h$$

These are the reactants that will be used in the syntheses of the amino acids, leucine, isoleucine and proline.

The total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for some of these stable molecules 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
Methyl diacetylene(2)	-192.16934	0.06934
Mg.methyl diacetylene.porphin(3)	-1377.31505	0.35932
diacetylene (4)	-153.00240	0.04203
Mg.diacetylene.porphin (5)	-1338.13417	0.32843
Mg.CO.porphin (6)	-1298.13452	0.29942
Mg.porphin.CO (7)	-1297.93784	0.30434
L-leucine (non-zwitterion)(8)	-440.26501	0.20796
L-isoleucine (non-zwitterion)(9)	-440.26559	0.20794
L-norleucine (non-zwitterion) (10)	-440.26648	0.20817
Mg-1, 2-amino pent-1,3-diyn-1yl.porphin (11)	-1433.62989	0.40324
Mg.1,3-amino pent-1-yne-3-ene-1-yl.porphin (12)	-1433.69366	0.40245
Mg.1,2-methyl bicycle[1.1.0] but-1-dehydro-1-en-4yl.porphin (13)	-1377.22809	0.35678
Mg.1,(2-didehydro-3-dehydro 3-methyl cyclopropenyliden-1yl) methan-1yl.porphin (14)	-1377.21615	0.35551
Mg.1,2-didehydro-3-dehydroethyliden-1yl cyclopropan-1yl.porphin(15)	-1377.21941	0.35513

Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin (16)	-1378.43219	0.38281
Mg.1,3-methenyl butyn-1-yl.porphin (17)	-1374.59087	0.38431
Mg.1,2-amino 3-methenyl butyn-1-yl.porphin (18)	-1434.86584	0.42952
Mg.1,3-(1-methenyl ethyl) 1H aziridin-2yl.porphin(19)	-1434.86399	0.42924
Mg.1,3-methenyl butanimin-1yl.porphin(20)	-1434.94414	0.42832
3-methenyl butanimine (21)	-249.78846	0.14028
Mg.1,3-methenyl butanimin-1-yl.porphin.CO(22)	-1547.93017	0.43879
Mg.1,(2-methenyl propyl) aziridine-3-one-1-yl.porphin(23)	-1547.94954	0.43870
CO	-113.02122	0.00556
H ₂ O	-76.19685	0.02298
NH ₃	-56.35421	0.03700
H ₂	-1.14414	0.01059

3.3 The overall stoichiometry for the formation of L-leucine, L-isoleucine and L-norleucine.

Although Mg.porphin is here taken as the catalyst for the reaction, the overall stoichiometry to form the amino acids, L-leucine, L-isoleucine and L-norleucine are as follows,

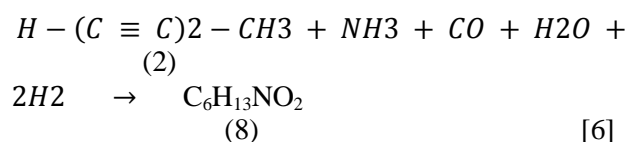


Fig.3 L-leucine (non-zwitterion) (8)

$$\Delta H = -0.18893 h$$

L-isoleucine(non-zwitterion) (9)

$$\Delta H = -0.18952 h$$

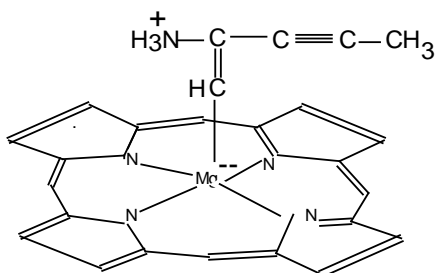
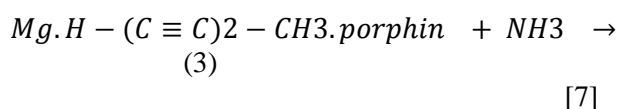
L-norleucine(non-zwitterion) (10)

$$\Delta H = -0.19093 h$$

The enthalpy changes are negative indicating that this may be the energetically favourable route to the initial formation of the amino acids. The intermediates by which these stoichiometric reactions may have occurred are as follows:

3.4 The formation of Mg.1, 2-amino pent-1,3-diyn-1yl.porphin.

The first reaction in this synthesis is probably not the reaction of Mg,1,methyl diacetylene.porphin with ammonia, as shown,



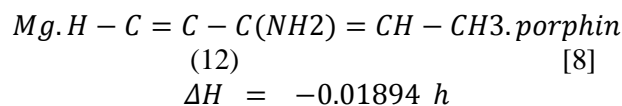
Mg,1,2-amino pent-1,3-diyne-1yl.porphin. (11)

Although this is the rate determining step in the prebiotic synthesis of most of the amino acids [17-21,32] this enthalpy change is the largest encountered and implies a large activation energy and the formation of a high energy compound.

$$\Delta H = 0.04553 \text{ h}$$

The activation energies for the forward and reverse reactions were calculated as 0.041 h and 0.001 h, respectively at MP2 accuracy.

There is also a more favourable enthalpy change for the addition of ammonia across the triple bond of the adduct than addition to C2 of the adduct and subsequent reaction to form a cyclic aziridine as shown later,

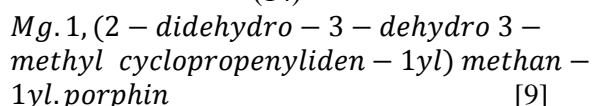
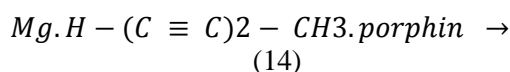
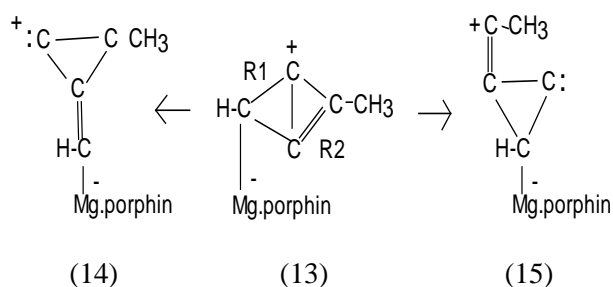


These initial calculations are not favourable for the formation of substantial concentrations of norleucine, 2-amino hexanoic acid, compared to the other isomers.

Similarly, the isomer, ψ -leucine, 2-amino-3,3-dimethyl butyric acid, cannot form as there is not any possible alkyne hydrocarbon to react with the catalyst.

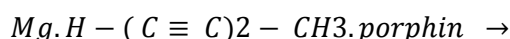
3.5 The formation of cyclic isomers of Mg,1,methyl diacetylene.porphin.

Here, it is postulated that the formation of the amino-acids L-leucine and L-isoleucine was initiated by photochemical excitation of the adduct Mg,1,methyl diacetylene.porphin. to form a bicyclic high energy product (13). The activation energy was calculated as 0.085 h. This may dissociate into two products of almost identical energy with both being inter-convertible via the marginally more stable molecule, Mg,1,2-methyl bicyclo[1.1.0] but-1-dehydro-1-en-4yl.porphin (13). The following structures depict these molecules. with a stereochemistry determined by the presence of the magnetic field pointing upwards from the porphin ring such that the positive charges of the adduct tended to move counterclockwise whilst the negative charges moved clockwise. For Mg,1,(2-didehydro-3-dehydro 3-methyl cyclopropenyliden-1yl) methan -1yl.porphin the adduct retains a positive charge of 0.08 with the only positively charged carbon atom of the adduct (C diradical) being 0.018. For Mg,1,(2-didehydro-3-dehydroethyliden-1yl) cyclopropan-1yl.porphin the adduct has a charge of 0.08 with the only positively charged carbon atom of the adduct (C radical) being 0.057. For each the only carbon atoms with positive charges, 0.018 and 0.057, respectively, move counter clockwise when viewed from above. giving rise to the structures shown.



$$\Delta H = 0.09551 \text{ h}$$

The activation energy to dissociate the bicyclic complex is 0.041 h and to form the complex 0.002 h.



Mg.1,2 – didehydro – 3 – dehydroethyliden – 1yl cyclopropan – 1yl.porphin
(15) [10]

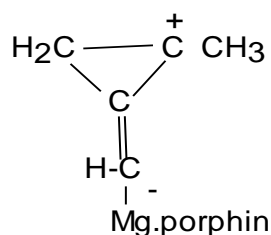
$$\Delta H = 0.09191 \text{ h}$$

The activation energy to dissociate the bicyclic complex is 0.051 h and to form the complex 0.020 h.

3.6 The formation L-leucine from Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin

The Mg.1,(2-didehydro 3-dehydro 3-methyl cyclopropenyliden-1yl) methan-1yl.porphin is a high energy diradical which would be much stabilized by atmospheric hydrogenation.

Mg.1, (2 – didehydro 3 – dehydro – 3 – methyl cyclopropenyliden – 1yl) methan – 1yl.porphin + H₂ →



Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin (16) [11]

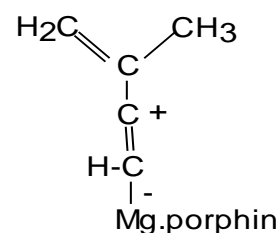
$$\Delta H = -0.05703 \text{ h}$$

The activation energy to form the carbon-hydrogen bond was found to be, 0.036 h, whilst the energy to restore the hydrogen-hydrogen bond was 0.091 h.

3.7 The formation of Mg.1,3-methenyl but-1-yl.porphin

With only moderate activation energy the Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin may isomerise to give Mg.1,3-methenyl butyn-1-yl.porphin

Mg.1, (2 – dehydro – 2 – methyl cyclopropenyliden – 1yl) methan – 1yl.porphin
(16) →



Mg.1,3-methenyl butyn-1-yl.porphin (17) [12]

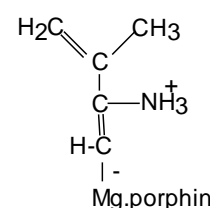
$$\Delta H = -0.09354 \text{ h}$$

The activation energy to open the ring was calculated as 0.024 h, whilst that to close it was 0.103 h.

3.8 The formation of Mg.1,2-amino 3-methenyl butyn-1-yl.porphin

The Mg.1,3-methenyl butyn-1-yl.porphin may react with ammonia gas at the positively charged C2 of the adduct. This is the rate determining step in the synthesis.

Mg.1,3 – methenyl butyn – 1 – yl.porphin + NH₃ →



Mg.1,2-amino 3-methenyl butyn-1-yl.porphin (18) [13]

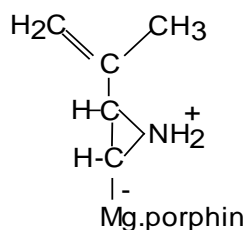
$$\Delta H = 0.02275 \text{ h}$$

The activation energy to add the ammonia was calculated as 0.028 h and 0.036 for the reverse reaction.

3.9 The formation of Mg.1,3-(1-methenyl ethyl) 1H aziridin-2yl.porphin

The Mg.1,2-amino 3-methenyl butyn-1-yl.porphin may cyclise to an aziridine derivative during being activated to transfer a hydrogen atom. The enthalpy change is marginal.

Mg.1,2 – amino 3 – methenyl butyn – 1 – yl.porphin →



Mg.1,3-(1-methenyl ethyl) 1H aziridin-2yl.porphin (19) [14]

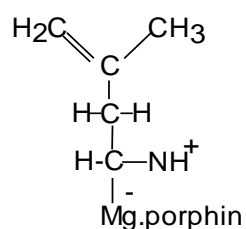
$$\Delta H = 0.00161 h$$

The activation energy to form the ring was calculated as 0.099 h, whilst that to close it was 0.093 h.

3.10 The formation of Mg.1,3-methenyl butanimin-1-yl.porphin

With only moderate activation energy a second hydrogen may be transferred from the protonated imino group to form the second carbon-hydrogen bond and opening the aziridine ring, as shown.

Mg.1,3 – (1 – methenyl ethyl) 1H aziridin – 2yl.porphin →



Mg.1,3-methenyl butanimin-1-yl.porphin (20) [15]

$$\Delta H = -0.08097 h$$

The activation energy to open the ring was calculated as 0.109 h, whilst that to close it was 0.205 h.

At the transition state the metal bonding changes from Mg-C to Mg-N. The imine is expected to dissociate to a minor extent with a small vapour pressure, but this requires a small activation energy according to the equation,

Mg.1,3 – methenyl butanimin – 1-yl.porphin → Mg.porphin + 3 – methenyl butanimine (21) [16]

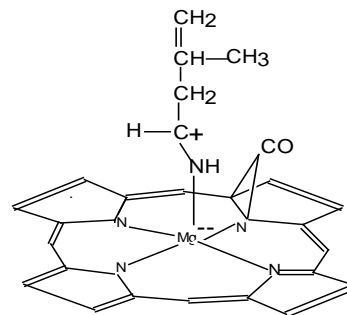
$$\Delta H = 0.03726 h$$

3.11 The formation of Mg.1,3-methenyl butanimin-1-yl.porphin.CO

For the correct formation of the L-isomer the 3-methenyl butanimine needs to chelate to the magnesium ion on a Mg.porphin which has already obtained the correct orientation of a bound carbon monoxide molecule [22], as shown,

Mg.porphin.CO + 3 – methenyl butanimine (7) (21)

→



Mg.1,3-methenyl butanimin-1-yl.porphin.CO (22) [17]

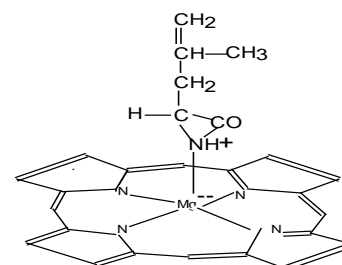
$$\Delta H = -0.20906 h$$

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

3.12 The formation of Mg.1,(2-methenyl propyl) aziridine-3-one-1-yl.porphin.

The Mg.1,3-methenyl butanimin-1-yl.porphin.CO may easily rearrange to form Mg.1,(2-methenyl propyl) aziridine-3-one-1-yl.porphin.

Mg.1,3 – methenyl butanimin – 1 – yl.porphin.CO → (22)



Mg.1,(2-methenyl propyl) aziridine-3-one-1-yl.porphin.(23) [18]

The enthalpy change is favourable.

$$\Delta H = -0.01946 h$$

The activation energy to form the aziridine was 0.093 h and the ring dissociation activation energy of 0.147 h.

3.13 The formation L-leucine.

Hydrolysis and hydrogenation in the reducing environment of the complex, is here depicted as releasing from the catalyst the non-zwitterionic form of L-leucine, Fig.3. Further formation of the zwitterion may occur.

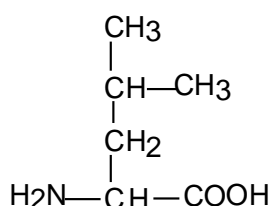
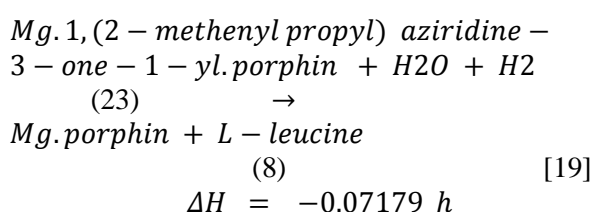
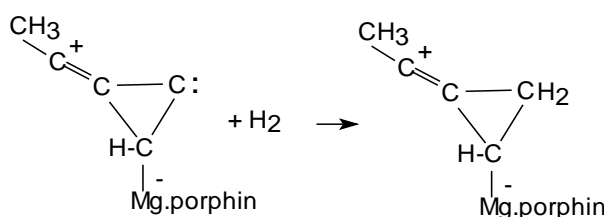
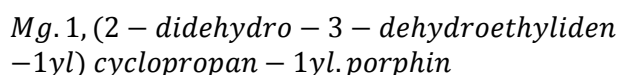


Fig.3 L-leucine (non zwitterion) (8)

3.14. The formation of L-isoleucine.

The proposed synthesis of L-isoleucine starts with the hydrogenation of the other cyclic high energy compound from the photolysis of Mg.H-(C \equiv C)₂-CH₃.porphin, Mg.1,(2-didehydro-3-dehydroethyliden-1yl) cyclopropan-1yl.porphin to give Mg.1,2-ethylidenyl cyclopropan-1yl.porphin, and proceeds in an identical manner.



$$(15) \quad [20]$$

Mg.1,(2-dehydroethylidenyl cyclopropan-1yl.porphin(24)

$$\Delta H = -0.05225 h$$

The activation energy for the addition was calculated as 0.089 h and 0.121 h for the reverse reaction.

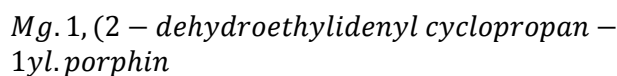
The total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for some of these stable molecules are given in Table 2.

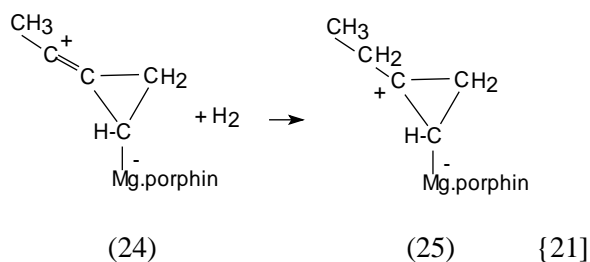
Table 2
MP2 /6-31G* total energies and zero point energies (hartrees) for the respective equilibrium geometries

Molecule	MP2 hartree	ZPE (HF) hartree
Mg.1,(2-dehydroethylidenyl cyclopropan-1yl.porphin (24)	-1378.42926	0.38084
Mg.1,2- dehydro 2-ethyl cyclopropan-1yl.porphin (25)	-1379.69479	0.40982
Mg.1,2-amino 2-ethyl cyclopropan-1yl.porphin(26)	-1436.02905	0.45425
Mg.1,3-ethyl 3-methyl 1H aziridin-2yl.porphin(27)	-1436.06973	0.45377
Mg.1, 2-methyl butanimin-1yl.porphin (28)	-1436.15250	0.45396
2-methyl butanimine(29)	-250.98865	0.16548
Mg.1,2-methyl butanimin-1-yl.porphin.CO (30)	-1549.14088	0.46451
Mg.1,2-(1-methyl propyl) aziridine-3-one-1-yl.porphin (31)	-1549.15132	0.46429

3.15. The formation of Mg.1,2-dehydro 2-ethyl cyclopropan-1yl.porphin

The Mg.1,(2-dehydroethylidenyl cyclopropan-1yl.porphin may undergo a further highly favourable hydrogenation to give Mg.1,2-dehydro 2-ethyl cyclopropan-1yl.porphin.



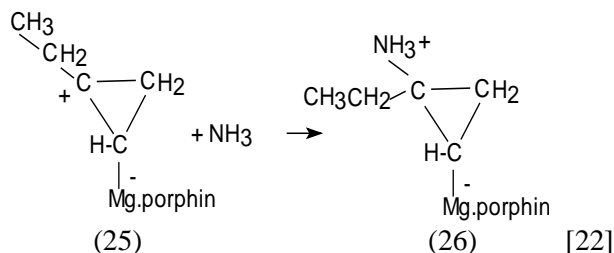


$$\Delta H = -0.10504 h$$

The activation energy for the addition was calculated as 0.044 h and 0.176 h for the reverse reaction

3.16. The formation of Mg,1,2-amino 2-ethyl cyclopropan-1yl.porphin

The Mg,1, 2-dehydro 2-ethyl cyclopropan-1yl.porphin may add ammonia to give Mg,1,2-amino 2-ethyl cyclopropan-1yl.porphin.



This is the rate determining step where the enthalpy change is comparable to that found for the formation of other amino acids [17-21] and less than that for the formation of norleucine.

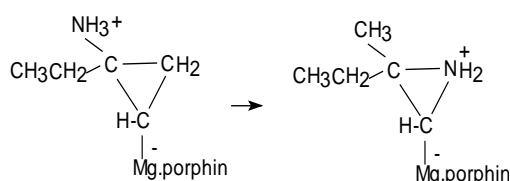
$$\Delta H = 0.02657 h$$

Also, the activation for the addition is lower, 0.019 h, and for the dissociation, 0.013 h.

3.17. The formation of Mg,1,3-(2-ethyl 2-methyl) 1H aziridin-2yl.porphin

The Mg,1,2-amino 2-ethyl cyclopropan-1yl.porphin may cyclise to an aziridine derivative, Mg,1,3-ethyl 3-methyl 1H aziridin-2yl.porphin, during being activated to transfer a hydrogen atom. The enthalpy change is favourable.

Mg, 1,2 – amino 2 – ethyl cyclopropan – 1yl.porphin



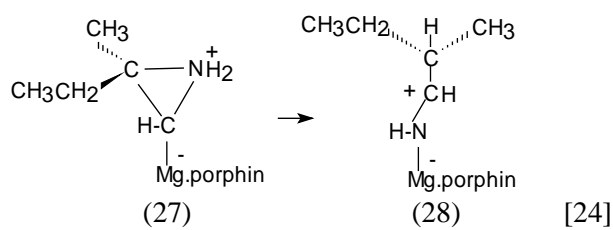
$$\Delta H = 0.04110 h$$

To determine the activation energy to form an aziridine, the potential energy surface studied involved the stretching of the CH –CH₂ bond of the cyclopropane ring and the stretching of the CH₂ – H(NH₂) bond.

The activation for the cyclisation was , 0.121 h, and for the reverse reaction, 0.087 h.

3.18. The formation of Mg,1, 2-methyl butanimin-1yl.porphin

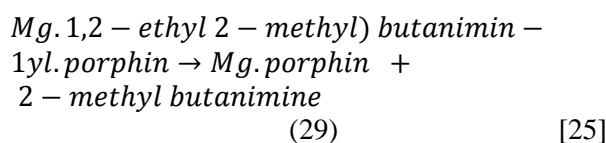
With only moderate activation energy a second hydrogen may be transferred from the protonated imino group to form the second carbon-hydrogen bond and opening the aziridine ring, as shown to give Mg,1,2-methyl butanimin-1 yl.porphin



$$\Delta H = -0.08261 h$$

The activation for the ring opening was , 0.087 h, and for the reverse reaction, 0.136 h.

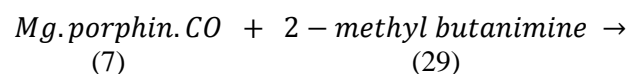
At the transition state the metal bonding changes from Mg-C to Mg-N. The imine is expected to dissociate to a minor extent with a small vapour pressure, but this requires a small activation energy according to the equation,

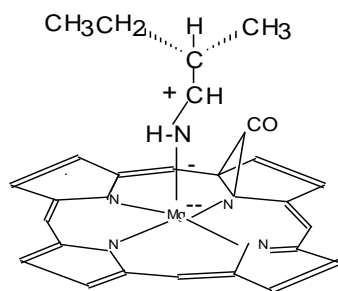


$$\Delta H = 0.04504 h$$

3.19. The formation of Mg,1,2-methyl butanimin-1-yl.porphin.CO

For the correct formation of the L-isomer the 2-methyl butanimine needs to chelate to the magnesium ion on a Mg.porphin which has already obtained the correct orientation of a bound carbon monoxide molecule [22], as shown,





Mg,1,2-methyl butanimin-1-yl.porphin.CO
(30) [26]
 $\Delta H = -0.21912 h$

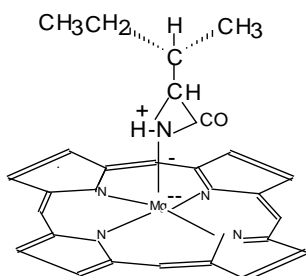
3.20. The formation of Mg,1,2-(1-methyl propyl) aziridine-3-one-1-yl.porphin.

The Mg,1,2-methyl butanimin-1-yl.porphin.CO may easily rearrange to form Mg,1,2-(1-methyl propyl) aziridine-3-one-1-yl.porphin with an activation energy of 0.105 h and a ring dissociation energy of 0.100 h.

The enthalpy change is marginal.

$$\Delta H = 0.01073 h$$

Mg,1,3 – methenyl butanimin –
1 – yl.porphin.CO →
(30)



Mg,1,2-(1-methyl propyl) aziridine-3-one-1-yl.porphin (31) [27]

3.21. The formation L-isoleucine.

Hydrolysis and hydrogenation in the reducing environment of the complex, is here depicted as releasing from the catalyst the non-zwitterionic form of L-isoleucine. Fig.4. Further formation of the zwitterion may occur.

Mg,1,2 – (1 – methyl propyl) aziridine –
3 – one – 1 – yl.porphin + H₂O →
(31)

Mg.porphin + L – isoleucine
(9) [28]

$$\Delta H = -0.02800 h$$

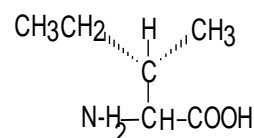


Fig.4 L-isoleucine (non zwitterion) (9)

3.22. The overall stoichiometry for the formation of L-proline.

Although Mg.porphin is here taken as the catalyst for the reaction, the overall stoichiometry to form the amino acid, L-proline is as follows,

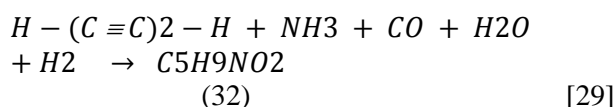


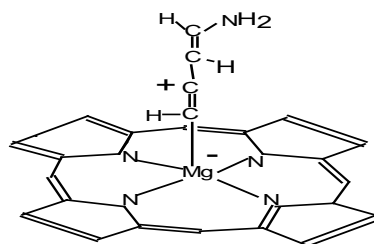
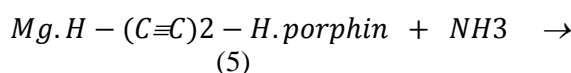
Fig.7.proline (non-zwitterion)

$$\Delta H = -0.17397 h$$

The enthalpy change is negative indicating that this may be the energetically favourable route to the initial formation of the amino acid. The intermediates by which this stoichiometric reaction may have occurred are as follows:

3.23. The formation of trans Mg,1-(4-amino but-3-en-1-yl) .porphin

The Mg.porphin coordinated diacetylene complex may react with ammonia to give an amine derivative, as follows:



Mg,1,(4-amino but-3-en-1-yl) .porphin
(33) [30]

$$\Delta H = -0.04449 h$$

The activation energy for the addition has been calculated as 0.049 h, and the activation energy for the reverse reaction as 0.109 h. However, this reaction tends to be non-specific with regard to forming 4-amino but-3-en-1-yl, and 3-amino but-3-en-1-yl [43], suggesting that more specific reactants would also be acceptable in this synthesis,

Mg.1,2 – didehydro – 3 – dehydroethyliden – 1yl cyclopropan – 1yl.porphin

(15) [10]

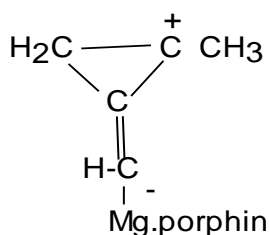
$$\Delta H = 0.09191 \text{ h}$$

The activation energy to dissociate the bicyclic complex is 0.051 h and to form the complex 0.020 h.

3.6 The formation L-leucine from Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin

The Mg.1,(2-didehydro 3-dehydro 3-methyl cyclopropenyliden-1yl) methan-1yl.porphin is a high energy diradical which would be much stabilized by atmospheric hydrogenation.

Mg.1, (2 – didehydro 3 – dehydro – 3 – methyl cyclopropenyliden – 1yl) methan – 1yl.porphin + H2 →



Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin (16) [11]

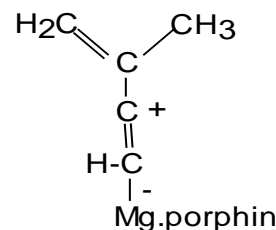
$$\Delta H = -0.05703 \text{ h}$$

The activation energy to form the carbon-hydrogen bond was found to be, 0.036 h, whilst the energy to restore the hydrogen-hydrogen bond was 0.091 h.

3.7 The formation of Mg.1,3-methenyl but-1-yl.porphin

With only moderate activation energy the Mg.1,(2-dehydro-2-methyl cyclopropenyliden-1yl) methan-1yl.porphin may isomerise to give Mg.1,3-methenyl butyn-1-yl.porphin

Mg.1, (2 – dehydro – 2 – methyl cyclopropenyliden – 1yl) methan – 1yl.porphin (16) →



Mg.1,3-methenyl butyn-1-yl.porphin (17)

[12]

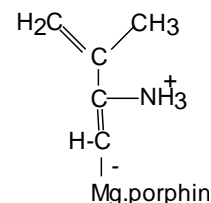
$$\Delta H = -0.09354 \text{ h}$$

The activation energy to open the ring was calculated as 0.024 h, whilst that to close it was 0.103 h.

3.8 The formation of Mg.1,2-amino 3-methenyl butyn-1-yl.porphin

The Mg.1,3-methenyl butyn-1-yl.porphin may react with ammonia gas at the positively charged C2 of the adduct. This is the rate determining step in the synthesis.

Mg.1,3 – methenyl butyn – 1 – yl.porphin + NH3 →



Mg.1,2-amino 3-methenyl butyn-1-yl.porphin (18)

[13]

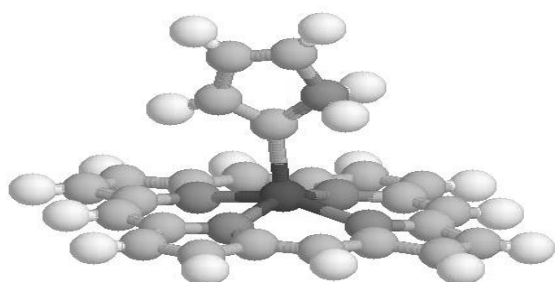
$$\Delta H = 0.02275 \text{ h}$$

The activation energy to add the ammonia was calculated as 0.028 h and 0.036 for the reverse reaction.

3.9 The formation of Mg.1,3-(1-methenyl ethyl) 1H aziridin-2yl.porphin

The Mg.1,2-amino 3-methenyl butyn-1-yl.porphin may cyclise to an aziridine derivative during being activated to transfer a hydrogen atom. The enthalpy change is marginal.

Mg.1,2 – amino 3 – methenyl butyn – 1 – yl.porphin →



(10) [33]

Fig.5. The optimized complex Mg.1,(1H-pyrrol-2-yl).porphin. (35)

The enthalpy change is favourable.

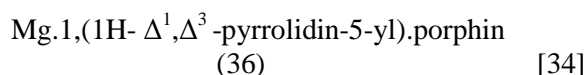
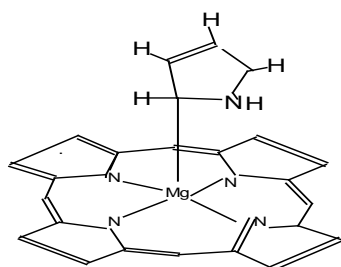
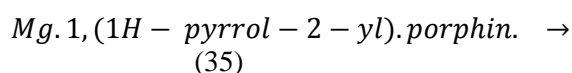
$$\Delta H = -0.02671 h$$

The activation energy for the prototropic shift was found to be, 0.100 h, whilst the activation energy for the reverse reaction was 0.127 h.

If the elements of water did add across the C3-C4 of the adduct at this time in the synthesis the charges -0.29 and -0.15, respectively, would have been expected to give the precursor to 4-hydroxy L-proline rather than 3-hydroxy L-proline.

3.26. The formation of Mg.1,(1H- Δ^1,Δ^3 -pyrrolidin-5-yl).porphin

The further prototropic shift on the Mg.1,(1H-pyrrol-2-yl).porphin from the quaternary nitrogen to the ring carbon-2 yields a 5-pyrrolidine adduct.



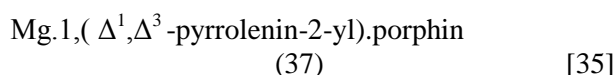
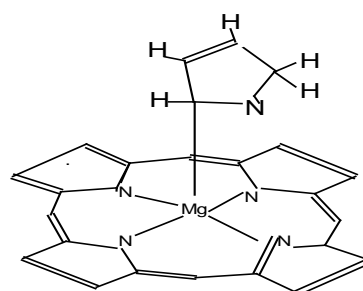
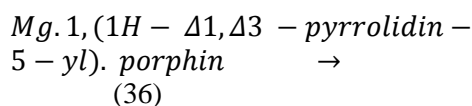
The enthalpy change is favourable.

$$\Delta H = -0.10908 h$$

The activation energy to form the carbon-hydrogen bond was found to be, 0.045 h, whilst the energy to restore the nitrogen-hydrogen bond was 0.132 h.

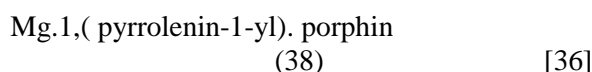
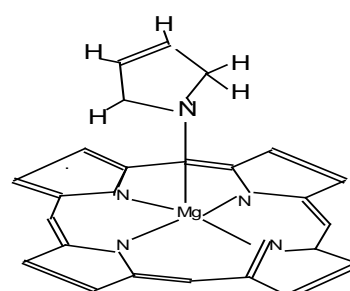
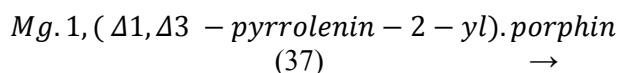
3.27. The formation of Mg.1,(pyrrolenin-2-yl).porphin

With only moderate activation energy a second hydrogen atom may be transferred from the imino group of the Mg.1,(1H- Δ^1,Δ^3 -pyrrolidin-5-yl).porphin to form the pyrrole imine adduct Mg.1,(Δ^1,Δ^3 -pyrrolidin-2-yl).porphin



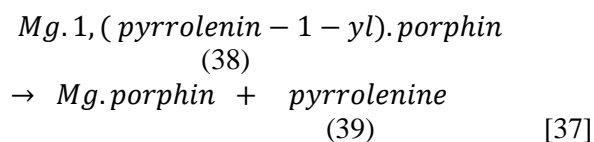
$$\Delta H = 0.02998 h$$

The activation energy for the proton shift was calculated as 0.098 h, whilst that for the reverse reaction was 0.105 h. At the transition state the metal bonding changes from Mg-C to Mg-N.



$$\Delta H = -0.02212 h$$

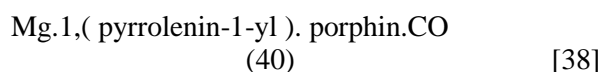
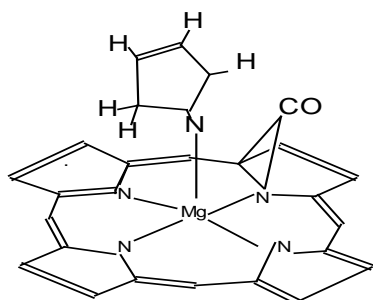
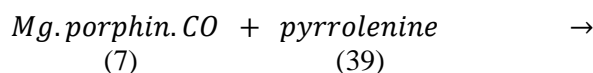
The imine is expected to dissociate to a minor extent with a small vapour pressure, but this requires a small activation energy according to the equation,



$$\Delta H = 0.04874 \text{ h}$$

3.28. The formation of Mg.1,(pyrrolenin-1-yl). porphin.CO

For the correct formation of the L-isomer the pyrrolenine needs to chelate to the magnesium ion on a Mg.porphin which has already obtained the correct orientation of a bound carbon monoxide molecule [22], as shown,



$$\Delta H = -0.21501 \text{ h}$$

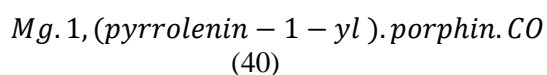
The enthalpy change is favourable and the activation energy to form van der Waals complexes is usually not significant if they are spontaneous.

3.29. The formation of Mg.1,(bicyclo - 1:5 pyrrolenin aziridine-2one) N-1-yl. porphin.

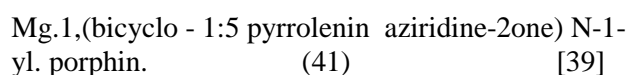
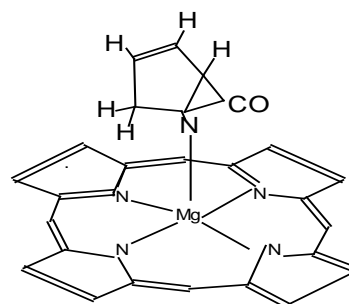
The Mg.1,(pyrrolenin-1-yl). porphin.CO may easily rearrange to form Mg.1,(bicyclo - 1:5 pyrrolenin aziridine-2one) N-1-yl. porphin, with an activation energy of 0.027 h and a ring dissociation energy of 0.073 h.

The enthalpy change is favourable.

$$\Delta H = -0.00335 \text{ h}$$



→



The reverse of this addition reaction occurs in the photolysis of aziridinediones to give isocyanate and carbon monoxide [46], and cyclopropanones to give enes and carbon monoxide [47].

3.30. The formation 3,4 didehydro L-proline.

Hydrolysis and hydrogenation, in the reducing environment of the complex, is here depicted as releasing the undissociated acid, Fig.7, from the catalyst. Further formation of the zwitterion may occur.

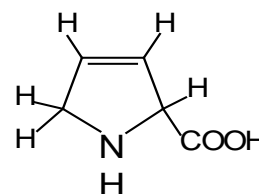
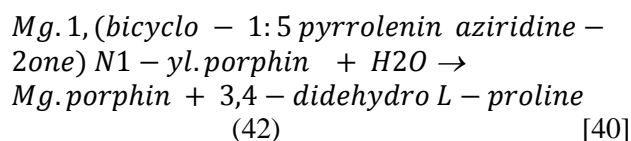


Fig.6. 3,4-didehydro L-proline (42)

$$\Delta H = -0.02217 \text{ h}$$

Further hydrogenation yields L-proline, as shown in Fig.7.

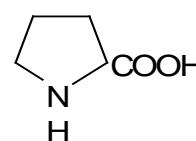
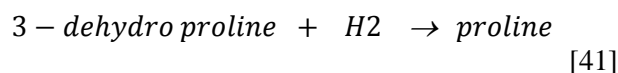


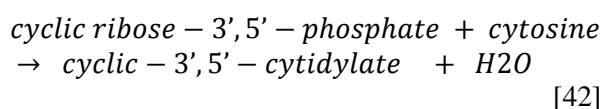
Fig.7 L- proline (32)

$$\Delta H = -0.0438 \text{ h}$$

3.30.1. The Method to Determine the Interaction Energies in L-proline⁺ acyl cyclic-3',5'-cytidylate

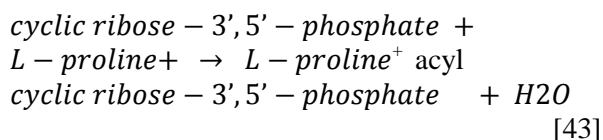
In order to explain why the CCC codon gives L-proline in protein synthesis [1], it has been postulated that L-proline, or its derivatives, came into close proximity and formed strong complexes resulting in them preferentially being associated in a prebiotic environment [48]. However, the interaction found in L-proline acyl cyclic-3',5'-cytidylate was only -0.00777 h, and this would be much reduced in an aqueous medium. However, the pKa of L-proline may be effectively increased if a local acceptor is present for the proton.

The following illustrates the method used [48] to determine the interaction energy values for 3,4-didehydro L-proline which may have been a precursor to L-proline. The approach taken here is to determine the total enthalpy changes for the following reactions:



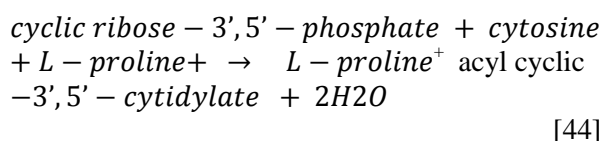
$$\Delta H_1 = -0.00594 \text{ h}$$

and,



$$\Delta H_2 = 0.02078 \text{ h}$$

The combined reaction is:



$$\Delta H_3 = -0.03646 \text{ h}$$

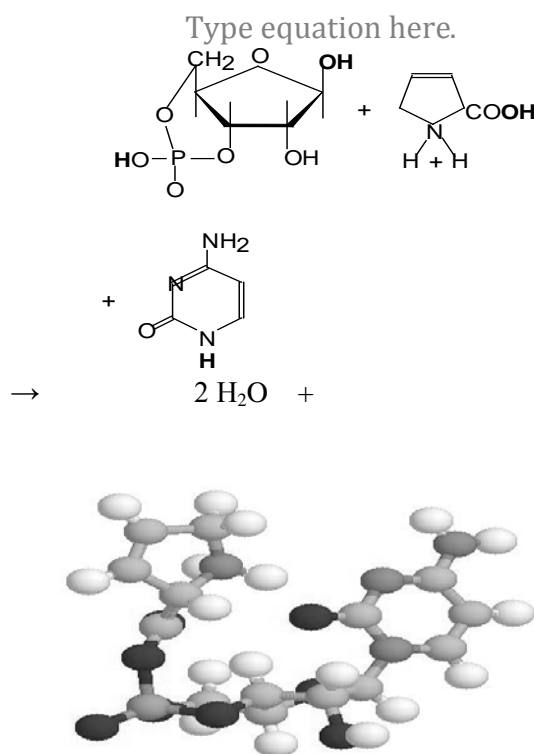
It is this last reaction that could allow for an intramolecular interaction between the cytosine and L-proline entities, here designated ΔH_4 . This interaction needs to be appreciable. As an approximate estimate it should be possible to write,

$$\Delta H_1 + \Delta H_2 + \Delta H_4 = \Delta H_3$$

provided the conformations do not change too much in forming the van der Waals complex. To this end, the conformation of the cytosine cyclic-3',5'-phosphate was held fixed, the same as in the complex, save for the added phosphate -H group

which was allowed to vary. Similarly, the conformation of the 3,4-didehydro L-proline⁺ acyl cyclic ribose-3',5'-phosphate was held fixed, the same as in the complex, save for the added -OH group which was allowed to vary as shown in Fig.8. By determining the enthalpy changes for these three separate reactions a reliable estimate of the base amino-acid interaction, ΔH_4 , can be obtained. Clearly the conformations of the cyclic cytosine-3',5'-phosphate, and 3,4-didehydro L-proline⁺ acyl cyclic ribose-3',5'-phosphate, when largely fixed in conformation may not be optimal. A certain input of energy may be required to form the complex. This may lead to excessive values for the formation of the glycosidic and phosphoacyl bonds. However, the advantage is a truer value of the enthalpy of interaction, ΔH_4 . It also seems likely, that as with most methods devised to partition the energy of a reaction that it is not theoretically rigorous.

$$\Delta H_4 = -0.05131 \text{ h}$$



[45]

Fig.8. The conformation of 3,4-didehydro L-proline⁺ acyl cyclic-3',5'-cytidylate

The data for these molecules are given in Table.4

Table 4

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

Molecule	MP2 hartree	ZPE (HF) hartree
cyclic ribose-3',5'-phosphate	-1061.38345	0.17729
cytosine	-393.76008	0.10555
cyclic-3',5'-cytidylate	-1378.95438	0.26604
3,4-didehydro L-proline ⁺	-399.07365	0.11378
3,4-didehydro L-proline ⁺ acyl cyclic ribose-3',5'-phosphate	-1384.26057	0.29604
3,4-didehydro L-proline ⁺ acyl cyclic ribose-3',5'-cytidylate	-1701.88743	0.33516

4. Conclusion

The presence of reactants, carbon monoxide, ammonia, alkynes and hydrogen in the early Earth's atmosphere may have been induced to react in thermodynamically and kinetically viable reactions such as those presented here to synthesise these unique amino acids from atmospherically formed imines in contrast to transition metal carbonylation [49]. The bicyclo - 1:5 pyrrolenin aziridine-2one may have reacted with cyclic ribose-3',5'-phosphate to form a rather stable L-proline acyl cyclic-3',5'-cytidylate that may have predisposed the origin of the present day codon for L- proline being CCC, CCU, CCG, and CCA [1].

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 APAC for facilities at the ANU and QMAS facilities at UQ, and the assistance of Mr.D.Green..

References:

- [1] A.L.Lehninger, *Biochemistry*,Worth, New York, 1975, pp.703,567,571,577,704,705.
- [2] E.H.Rodd.(ed), *Chemistry of Carbon Compounds*, Elsevier, Amsterdam,Vol.1B, 1952, pp.830,1338.
- [3] C.J.Li, D.M.Brawnsnson,T.J.Mabry, C.Perera, E.A.Bell, Non protein amino acids from seeds of

Cycas circinalis and *Phaseolus vulgaris*, *Phytochemistry*,42(2),1996, pp.443-445.

[4] L.Cvak, A.Jegorov, P.Sedmera, J.Cejka, B.Kratochvil, S.Pakhomova, *Amino Acids*,20(2),2005, pp.145-150.

[5] S.Bronco, C.Cappelli and S. Monti, Understanding the structural and binding properties of collagen: a theoretical perspective, *J. Phys. Chem. B*, 108(28), 2004, pp.10101-10112.

[6] R.Rai, S. Aravinda, K. Kanagarajadurai, S.Raghothama, N.Shamala and P.J. Balaram, Diproline templates as folding nuclei in designed peptides. Conformational analysis of synthetic peptide helices containing amino terminal pro-pro segments, *J. Am. Chem. Soc.*,126 ,2006, pp.7916-7928.

[7] B.Alberts, D.Bray, J.Lewis, M.Raff, K.Roberts and J.D.Watson, *Molecular Biology of the Cell*,3rd.Edition, Garland Publishing.New York, 115,1994, pp.979,984.

[8] J.B.Cohen and P.C.Austin, *Theoretical Organic Chemistry*, MacMillan, London,1954.

[9] E.E.Conn and P.K.Stumpf, *Outlines of Biochemistry*, John Wiley Inc.1972, pp71.

[10] C.R.Cantor and P.R.Schimmel, *Biophysical Chemistry*,Part 1, W.H.Freeman, San Francesco,1980.pp.49.

[11] T.A.Brown,Ed., *Molecular Biology LabFax*, BIOS Scientific publishers Ltd.,Oxford, U.K. 1991, pp.29.

[12] N.Aylward, and N.R.Bofinger, Possible origin for porphrin derivatives in prebiotic chemistry - a computational study, *Orig.Life Evol. Biosph.* vol.35(4),2005, pp345-368.

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

[14] R.B.Loren, A.Wootten, L.G.Mundy, The detection of interstellar methyl diacetylene, *Astrophysical Journal*, Part2,286,1984, pp.23-26.

[15] T.Oka, The infrared spectrum of H₃⁺ in laboratory and space plasmas, *Rev.Mod.Phys.*,64,1992, pp.1141-1149.

[16] 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.

[17] N.N. Aylward, A computational study of a prebiotic synthesis of L-histidine, in *WSEAS Proceedings of the 15 th. International Conference on Computers*, Eds. N.Mastorakis et.al.Corfu Island, 2011, pp.166-171.

[18] N.N. Aylward, A computational study of a prebiotic synthesis of L-arginine, in *WSEAS*

Proceedings of the 16 th. International Conference on Computers, Eds. S.Sendra and J.C.Metrolho, Kos Island, 2012, pp.321-325.

[19] N.N. Aylward, A computational study of a prebiotic synthesis of L-lysine, in *WSEAS Proceedings of the 16 th. International Conference on Computers*, Eds., S.Sendra and J.C.Metrolho.Kos Island, 2012, pp.336-331.

[20]] N. Aylward, A Computational study of a prebiotic synthesis of L-phenylalanine,in *WSEAS Proceedings of the 7th European Computing Conference (ECC '13)*, Eds., D.Boras, N. M Preradovic, F. Moya, M.Rushdy, A.M.Salem, Dubrovnik, 2013, pp.112-117.

[21] N. Aylward, A Computational Study of a Prebiotic Synthesis of L-Tryptophan,in *WSEAS Proceedings of the 7th European Computing Conference (ECC '13)*, Eds., D.Boras, N. M Preradovic, F.Moya,M.Rushdy, A.M.Salem, Dubrovnik, 2013, pp.105-111.

[22] 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.

[23] 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.

[24] M.P.Doyle, Catalytic methods for metal carbene transformations, *Chem. Rev.*, 86, 1986,pp. 919-39.
Chem. Rev.,96,1996, pp.2035-2052.

[25] A.R.Katritzky, O.Meth-Cohn, C.W.Rees, C.J.Moody (Ed.), *Comprehensive organic functional group transformations*. 5, Pergamon. 1995.

[26] J.P.Collman, L.S.Hegedus, J.R.Norton, R.G. Finke, "*Principles and Applications of Organotransition Metal Chemistry*", University Science Books, Mill Valey, California, ch.6,1987, pp.356.

[27] A.M.Tafesh and J.Weiguny, A review of the selective catalytic reduction of aromatic nitro compounds into aromatic amines, isocyanates, carbamates and ureas using CO, *Chem.Rev.*,6, 1996, pp.2035-2052.

[28] I.Fernandez and M.A. Sierra. β -lactams from Fischer carbene complexes: scope, limitations and reaction mechanism, *Top.Heterocyclic Chem.*, Springer-Verlag,Berlin,30, 2013, pp.65-84.

[29] M.S.Sigman and B.E.Eaton,The first iron-mediated carbon-nitrogen bond formation [4+1] cycloaddition of allenyl imines and carbon monoxide,*J.Org.Chem.*, 59, 1994, pp.7488-7491.

[30] F.Glorius, *N-heterocyclic carbenes in transition metal catalysis*, Springer,21,2007, pp.238.

[31] N.N.Aylward, *Studies of electronic and structural properties of molecular clusters of prebiotic importance*, Ph.D. Thesis, Queensland University of Technology,1995.

[32] 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.

[33] *Gaussian03, Users Reference*,Gaussian Inc.,Carnegie Office Park, Bldg.6., Pittsburgh, PA 15106, USA, 2003.

[34] W.J.Hehre, L.Random, P.V.R. Schleyer, and J.A.Pople, *Ab Initio Molecular Orbital Theory*, Wiley, New York, 1986.

[35] 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.

[36] P.W.Atkins, *Molecular Quantum Chemistry*, Clarendon Press, Oxford,1970.

[37] W.T.Simpson, On the theory of the π -electron system in porphins, *J.Chem.Phys.*,17, 1949, pp. 1218-1221.

[38] J.R.Platt, Classification of cata-condensed hydrocarbons, *J.Chem.Phys.*,17, 1949. pp.484-495.
[39] H.G.Longuet-Higgins, C.W.Rector,and J.R.Platt, Molecular orbital calculations on porphine and tetrahydroporphine, *J.Chem.Phys.*,18(9), 1950. pp.1174-1181.

[40] J.M.Anderson, *Introduction to Quantum Chemistry*, W.A.Benjamin.Inc.N.Y.1969.

[41] J.A.Pople, W.G.Schneider and H.J.Bernstein, *High-resolution Nuclear magnetic resonance*, McGraw-Hill Book Company, 1959.

[42] D.Mansuy, J.P.Battioni, D.Dupree, E.Santoni, *J.Am.Chem.Soc.*104, 1982, pp.6159-6161.

[43] C.Ingold, *Structure and Mechanism in Organic Chemistry*,Cornell Univ.Press,1953.

[44] M.Besev, Radical cyclisation approaches to pyrrolidines, *Acta Universitatis Upsaliensis*, Uppsala, 2002.

[45] P.S.Manona, J.L.Stavinoha, R.Swonson, Photochemistry of N-allyliminium salts. A novel photocyclisation reaction leading to pyrrolidines, *J.Am.Chem.Soc.*,99(20),1977, pp .6781-6792.

[46] F.Risi, L.Pizzala, M.Carles, P.Verloque and J.P.Aycard, Photolysed matrix isolated 4-R-1,2,4-

triazoline-3,5-diones:identification of aziridine-2,three-dimensional one transients, *J.Org.Chem.*, 61,1996. pp.666.

[47] W.Horspool, F.Leuci,(Eds.), *CRC Handbook of organic photochemistry and photobiology*, CRC Press.LLC.,2004.

[48] N.Aylward, Intramolecular Interactions in Amino Acyl Cyclic 3',5' Nucleotides. *J.Theoretical Biology*, 244, 2007, pp.258-274.