A Computational Study of a Prebiotic Synthesis of L-Tyrosine and L-Thyroxine (T3/T4)

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***Abstract*—** The magnesium ion metalloporphyrin complex is shown to bind the ligand diacetylene in weak van der Waals complexes on the metal and nitrogen sites. Photochemical excitation leads to a didehydrophenyl ethynyl complex which may add the elements of water. Further reaction with ammonia gives an amine that easily transforms to an aziridine derivative, and ultimately an imine 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 a substituted aziridine-2one that may easily hydrolyse to the zwitterionic form of the amino acid L-tyrosine. L-thyroxine (T3/T4) is formed by iodination of the precursors, 4-hydroxy phenyl ethynyl complex and 4-hydroxy phenyl complex followed by their interaction.

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

***Keywords*—** Prebiotic photochemical synthesis, L-tyrosine, L-thyroxine, L-triiodothyronine.

I. Introduction

L-tyrosine (Tyr,Y), a non-essential amino acid [1], is a common constituent of proteins [2]. It is an L-amino acid [1], with the pK_a of the carboxyl group recorded as 2.20, the amine group at 9.11, and the phenol group at 10.07 [1], so that it is present in solution as a zwitterion. The biosynthesis [1] in the body involves the addition of a hydroxyl group to L-phenylalanine catalyzed by the enzyme phenylalanine 4-monooxygenase. In plants, p-hydroxyphenylpyruvate is transaminated using glutamate as the nitrogen source to give tyrosine and α-ketoglutarate. The hydroxyl group of tyrosine may undergo phosphorylation or sulfation [3]. Tyrosine is converted to the signaling molecule L-3,4-dihydroxyphenylalanine , which is further converted into 3-hydroxytyramine (dopamine), noradrenaline, and adrenaline (epinephrine). The latter three are known as the catecholamines [4]. It also gives rise to the skin pigment melanin [5], and is present in the indole alkaloids [6]. The codons for L-tyrosine are UAU and UAC [1]. Several organic syntheses have been accomplished [6].

Thyroxine (L-3,5,3',5'-tetraiodothyronine), T4, and triiodothyronine (L-3,5,3'-triiodothyronine), T3, are both secreted by the thyroid gland where iodide is used to iodinate tyrosine through the action of a peroxidase to yield 3,5-diiodotyrosine, which is then converted into thyroxine and 3,5,3'-triiodothyronine [1]. Thyroxine has a profound effect on the basal metabolic rate of man and animals [1].

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 and hydrogen. It is also supposed that alkynes such as diacetylene were present as found on Titan, a moon of Saturn [9]. It has also been demonstrated that porphin may act as a catalyst for the formation of sugars [10] and polyenes [11].

This paper proposes a model for the catalytic photochemically activated formation of L-tyrosine from the gases, diacetylene, ammonia, carbon monoxide, hydrogen, and the catalyst magnesium porphin. The iodine is sourced from the Earth's crust to iodinate the tyrosine precursor.

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

2 Problem Formulation

This proposed computational study of a plausible synthesis of L-tyrosine and L-thyroxine 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 [12] commercial package. The standard calculations at the HF and MP2 levels including zero-point energy corrections at the Hartree Fock level [13], together with scaling [14], using the same basis set, 6-31G*, are as previously published [7]. To accommodate the iodine atom, the 6-31G* basis set was augmented with an extra basis set using Gaussian exponents, contraction coefficients and supplementary functions [15]. 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 [13], and activation energies calculated at the HF level without scaling are less accurate.

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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 [12].

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)

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 [16] 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.

Mg.porphin + H-$(C\equiv C)_2$-H $\rightarrow$ Mg.H-$(C\equiv C)_2$-H.porphin
(1) (2) (3) [1]

ΔH = -0.01480 h

However, it may also form a similar weak charge transfer complex of higher energy bonded to a peripheral pyrrole nitrogen atom [16]. It is assumed that this is formed from photochemical excitation. This is represented as,

Mg.porphin + H-$(C\equiv C)_2$-H $\rightarrow$ Mg.porphin.H-$(C\equiv C)_2$-H
(1) (2) (4) [2]

ΔH = -0.00274 h

The addition of a second diacetylene adduct slightly destabilises the di-adduct complex, as shown [16],

Mg.porphin + 2 H-$(C\equiv C)_2$-H $\rightarrow$ Mg.H-$(C\equiv C)_2$-H.
(1) (2) (5)
porphin.H-$(C\equiv C)_2$-H. [3]

ΔH = -0.01220 h

This is the first reactant required in the synthesis. Mg.porphin also forms a stable high energy complex with carbon monoxide in which the carbon monoxide is in a particular orientation on a peripheral pyrrole unit of the porphin [10]. This is also involved in the proposed synthesis, as shown later. The formation requires photochemical activation, which is less than the first ultraviolet excitation of the complex. The enthalpy of formation is positive.

Mg.porphin + CO $\rightarrow$ Mg.porphin.CO
(1) (6)

ΔH = 0.21136 h [4]

Mg.CO.porphin $\rightarrow$ Mg.porphin.CO
(7) (6) [5]

ΔH = 0.20106 h

The CO group is able to move through a transition state to the porphin ring where it forms an excited, but stable bridged aziridine-2one ring [10,17-18] at a pyrrole unit.

These are the reactants that will be used in the synthesis of the amino acid, tyrosine.

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
diacetylene (2)	-153.00240	0.04203
Mg.H-$(C\equiv C)_2$-H.porphin (3)	-1338.13417	0.32843
Mg..porphin.H-$(C\equiv C)_2$-H (4)	-1338.12537	0.29257
Mg.H-$(C\equiv C)_2$-H. porphin.H-$(C\equiv C)_2$-H (5)	-1491.13477	0.37136
Mg.porphin.CO (6)	-1297.93784	0.30434
Mg.CO.porphin (7)	-1298.13452	0.29942
L-tyrosine (non-zwitterion)(8)	-628.10367	0.20863
Mg.1,2-(3,4-didehydrophenyl) ethyn-1yl .porphin (9)	-1491.23263	0.37750
Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin (10)	- 1567.55637	0.40927
tetraacetylene (11)	-304.85205	0.06201
Mg. H-$(C \equiv C)_4$-H .porphin (12)	-1489.99743	0.35067
Mg.1,6-hydroxy-2,3,4,5-tetra-en 7-yl octa-1-yl. porphin$^-$(13)	-1565.63790	0.36321
Mg.1,6-hydroxy-2,3,4,5,7-penta-en octa-1-yl.porphin(14)	-1566.26462	0.38277
Mg.1,2-(6-hydroxy 2,3-didehydrophenyl)-ethyn-1-yl. porphin (15)	-1566.67922	0.39479
Mg.1,2-(3-dehydro 4-hydroxyphenyl) ethyn-1-yl.porphin (16)	-1566.90759	0.39290
Mg.1,2-amino 2-(4-hydroxyphenyl) ethen-1-yl.porphin (17)	-1623.89885	0.45469
Mg.1,3-(4-hydroxyphenyl) 1H aziridin-2-yl).porphin (18)	-1623.90333	0.45480
Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin (19)	-1623.97099	0.45386
2-(4-hydroxyphenyl) ethanimine (20)	-438.82312	0.16591
Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin.CO (21)	-1736.96470	0.46440
Mg.1,2-(4-hydroxyphenyl) methanyl aziridine-3-one-1-yl. porphin (22)	-1736.98441	0.50172

Mg.porphin.(H-C≡C-H)$_2$		
	-1339.19887	0.34579
CO	-113.02122	0.00556
H_2O	-76.19685	0.02298
NH_3	-56.35421	0.03700
H_3^+	-1.29643	0.02210
H_2	-1.14414	0.01059
OH^-	-75.51314	0.00885

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

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

2 H-(C≡C)$_2$-H + NH_3 + CO + 2H_2O →
$C_9H_{11}NO_3$ (8) [6]

Fig.2.tyrosine (non-zwitterion)

ΔH = -0.28490 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:

3.3 The formation of Mg.1,2-(3,4-didehydro phenyl) ethynyl .porphin

The two surface adducts of Mg.H-(C≡C)$_2$-H.porphin. H-(C≡C)$_2$-H, have very low barriers to rotation of less than 400 cal.[11] However, they cannot rotate past each other as the C3 of one adduct will collide with C1 of the other adduct. They spontaneously coalesce to reduce the energy of the complex without recorded activation energy. However, a typical Diels Alder reaction may result in a 1:4 addition to the other adduct. The most stable resulting adduct is bonded to the Mg ion, as shown in Fig.1,

Mg.H-(C≡C)$_2$-H.porphin. H-(C≡C)$_2$-H →
(5)

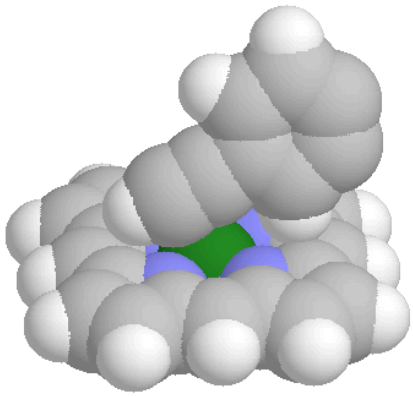


Fig.1. Mg.1,2-(3,4-didehydro phenyl) ethyn-1yl .porphin
(9) [7]

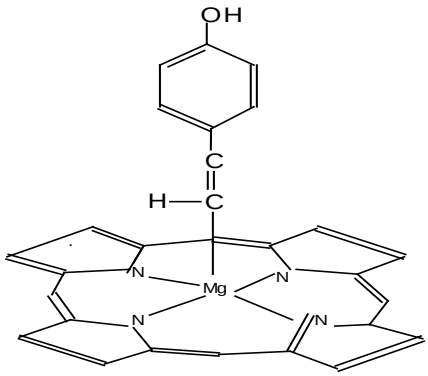
ΔH = -0.09240 h

The activation energy for the Mg.H-(C≡C)$_2$-H.porphin. H-(C≡C)$_2$-H to cyclise to a six membered ring was calculated as 0.061h by bringing the peripheral carbon atoms of the diacetylene coordinated to the N-pyrrole into close proximity with the C3 and C4 of the Mg coordinated bonded diacetylene, whilst the activation energy for the reverse reaction was 0.125 h.

3.4 The formation of Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin

The highly unsaturated Mg.1,(3,4-didehydrophenyl ethynyl) .porphin has a net adduct positive charge of 0.042, with formal electronic charges on the C5 and C6 of the adduct of -0.045 and -0.017, respectively. Atom C6 carries the least negative charge of all the aromatic ring carbon atoms. It is postulated that the molecule is predisposed to nucleophilic attack by hydroxyl anion at C6 and by proptonation at C5 of the adduct, as shown,

Mg.1,(3,4-didehydrophenyl ethyn-1yl) .porphin
(9) + H_2O →



Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin

(10) [8]

$\Delta H = -0.11907$ h

This has a highly favourable enthalpy change and no activation energy was calculated. for it.

3.4.1 The synthesis of Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin

If it is supposed that the molecule tetraacetylene was also present [19], apart from diacetylene, then an entirely equivalent synthesis of the Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin is feasible. The first reaction involves the formation of the parallel in-plane van der Waals complex, Mg.H-(C ≡ C)$_4$-H.porphin, with the catalyst, Mg.porphin, as follows,

$H\text{-}(C{\equiv}C)_4\text{-}H$ + Mg.porphin →

Mg. $H\text{-}(C{\equiv}C)_4\text{-}H$ .porphin

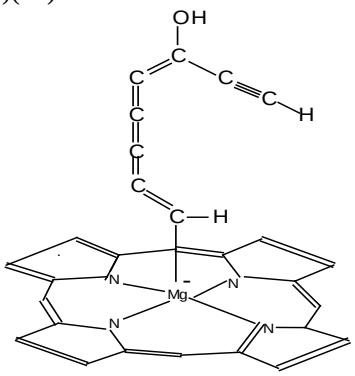
(11) (1) (12) [9]

$\Delta H = -0.02642$ h

In the triplet state the adduct has a net positive charge of 0.047 with positive charges on the adduct C6 and C7 of 0.364 and 0.314, respectively. It should be subject to nucleophilic attack by hydroxyl ion, as shown,

Mg. $H\text{-}(C{\equiv}C)_4\text{-}H$ .porphin + OH^{-1} →

(singlet)(12)



Mg.1,6-hydroxy-2,3,4,5-tetra-en 7-yl octa-1-yl. porphin$^-$

(13) [10]

$\Delta H = -0.12404$. h

No activation energy was recorded for this addition. It is completed with vigorous protonation of the molecule which can occur at C5 of the adduct,

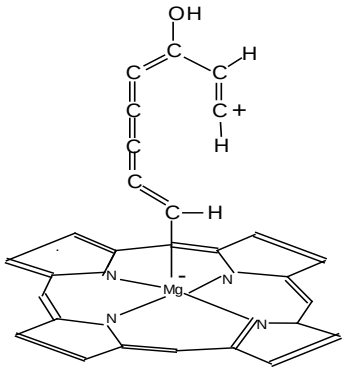
$\Delta H = -0.56863$ h

and on C7 of the adduct,

$\Delta H = -0.42784$ h

Both reactions are expected to occur.

Mg.1,6-hydroxy-2,3,4,5-tetra-en 7-yl octa-1-yl. porphin$^-$ + H^+ →

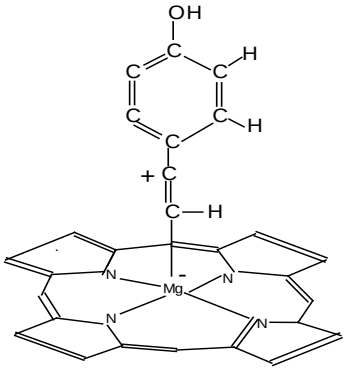


Mg.1,6-hydroxy-2,3,4,5,7-penta-en octa-1-yl.porphin(14)

[11]

The final closure of the ring is energetically favourable,

Mg.1,6-hydroxy-2,3,4,5,7-penta-en octa-1-yl.porphin →



Mg.1,2-(4-hydroxy 2,3-didehydrophenyl)-ethyn-1-yl. porphin(15) [12]

$\Delta H = -0.18147$ h

The activation energy to close the ring, involving bond rotation, was calculated as 0.019 h.

If the Mg.1,2-(4-hydroxy 2,3-didehydrophenyl)-ethyn-1-yl.porphin hydrogenates in the reducing atmosphere, then the Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin is formed.

Mg.1, Mg.1,2-(4-hydroxy 2,3-didehydrophenyl)-ethyn-1-yl. porphin (15) + H_2

→

Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin (10)

[13]

The hydrogenation is favourable,

$\Delta H = -0.13344$ h

In the mechanism above the protonation is placed before the hydrogenation as it is the more energetic of the reactions. Alternatively, the hydrogenation may precede the protonation, and this is followed by the protonation which leads to ring closure without activation energy if the correct rotomer is present.

The hydrogenation is as follows:

Mg.1,6-hydroxy-2,3,4,5-tetra-en 7-yl octa-1-yl. porphin$^-$ (13) + H_2 →

Mg.1,2-(3-dehydro 4-hydroxyphenyl) ethyn-1-yl.porphin (16) [14]

$\Delta H = -0.10854$ h

The ring forms during the optimization if the correct rotomer is present.

The subsequent protonation is as follows:

Mg.1,2-(3-dehydro 4-hydroxyphenyl) ethyn-1-yl.porphin (16) + H^+ →

Mg.1,2-(4-hydroxy-phenyl) ethyn-1yl .porphin (10) [15]

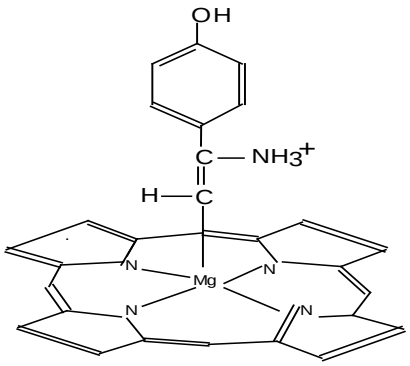
$\Delta H = -0.67737$ h

The enthalpy change for the formation of this reactant from tetraacetylene is the same as its formation from diacetylene.

3.5 The formation of Mg.1,2-amino 2-(4-hydroxyphenyl) ethen-1-yl.porphin

The Mg.1,2-(4-hydroxyphenyl) ethynyl .porphin may add ammonia in a weak reaction that is a rate determining step in the synthesis of amino acids [20-21].

Mg.1,2-(4-hydroxyphenyl) ethyn-1yl .porphin (10) + NH_3 →



Mg.1,2-amino 2-(4-hydroxyphenyl) ethen-1-yl.porphin (17) [16]

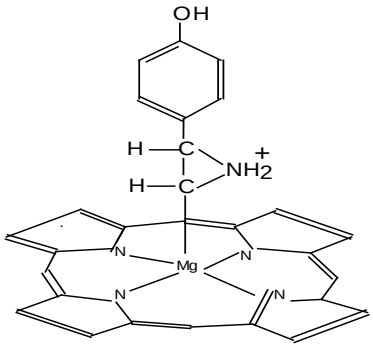
$\Delta H = 0.01922$ h

The activation energies for the forward and reverse reactions were calculated as 0.034h and 0.023 h, respectively.

3.6 The formation of Mg.1,3-(4-hydroxyphenyl) 1H aziridin-2-yl.porphin

The Mg.1,2-amino 2-(4-hydroxyphenyl) ethen-1-yl.porphin may cyclise to an aziridine derivative during being activated to transfer a hydrogen atom. The enthalpy change is marginally favorable.

Mg.1,2-amino 2-(4-hydroxyphenyl) ethen-1-yl.porphin → (17)



Mg.1,3-(4-hydroxyphenyl) 1H aziridin-2-yl.porphin. (18) [17]

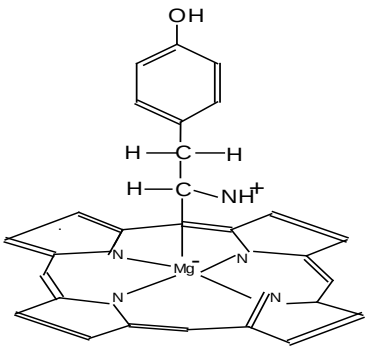
$\Delta H = -0.00438$ h

The activation energy to form the carbon-hydrogen bond was found to be, 0.055 h, whilst the energy to restore the nitrogen-hydrogen bond was 0.051 h. The aziridine ring forms during this first hydrogen transfer.

3.7 The formation of Mg.1,2-phenyl ethanimin-1-yl. porphin

With only moderate activation energy a second hydrogen atom may be transferred from the protonated amino group to form the second carbon-hydrogen bond and opening the aziridine ring [20-21], as shown.

Mg.1,3-(4-hydroxyphenyl) 1H aziridin-2-yl.porphin (18) →



Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin
(19) [18]
$\Delta H = -0.06850$ h

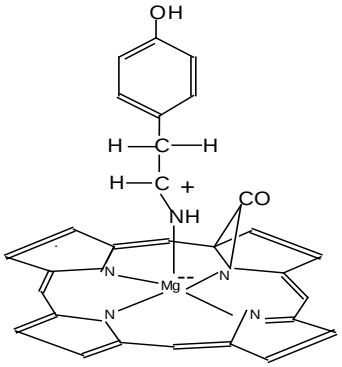
The activation energy to open the ring was calculated as 0.095 h, whilst that to close it was 0.195 h. These values are comparable to those previously found for the formation of the amino acids serine and threonine [20]. At the transition state the metal bonding changes from Mg-C to Mg-N. The imine is expected to dissociate to a minor extent with a small vapour pressure, but this requires a small activation energy according to the equation,

Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin
→
Mg.porphin + 2-(4-hydroxyphenyl) ethanimine
(20) [19]
$\Delta H = 0.04060$ h

3.8 The formation of Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin.CO

For the correct formation of the L-isomer the 2-(4-hydroxy-phenyl ethanimine needs to chelate to the magnesium ion on a Mg.porphin which has already obtained the correct orientation of a bound carbon monoxide molecule [10], as shown,

Mg.porphin.CO + 2-(4-hydroxyphenyl) ethanimine
(6) (20) →



Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin.CO
(21) [20]
$\Delta H = -0.22003$ h

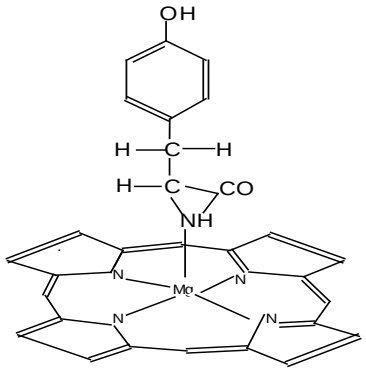
The enthalpy change is favourable and the activation energy to form van der Waals complexes is usually not significant if they are spontaneous.

3.9 The formation of Mg.1,2-(4-hydroxyphenyl) methanyl aziridine-3-one-1-yl.porphin.

The Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl.porphin.CO may easily rearrange to form Mg.1,2-(4-hydroxyphenyl) methanyl aziridine-3-one-1-yl).porphin.with an activation energy of 0.152 h and a ring dissociation energy of 0.150 h.

The enthalpy change is favourable.
$\Delta H = -0.01957$ h

Mg.1,2-(4-hydroxyphenyl) ethanimin-1-yl. porphin.CO
(21) →



Mg.1,2-(4-hydroxyphenyl) methanyl aziridine-3-one-1-yl.porphin**.** (22) [21]

3.10 The formation L-tyrosine.

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.1,2-(4-hydroxyphenyl) methanyl aziridine-3-one-1-yl. porphin $+ H_2O \rightarrow$ Mg.porphin + L-tyrosine
(8) [22]

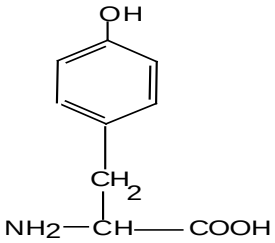


Fig.2 L-tyrosine (8)
$\Delta H = -0.01995$ h

3.11 The formation L-thyroxine.

The abundance of iodine in the igneous rocks of the crust of the Earth is 0.00003% [22]. In a mildly reducing atmosphere containing ammonia and a mildly alkaline environment, there may have been some concentrations of phosphonium and ammonium iodides. The former undergoes ready thermal dissociation to phosphine and hydrogen iodide [22]. The latter is characterised by volatility and facile disproportionation to

hydrogen and iodine vapour.

$$2HI \rightarrow H_2 + I_2 \qquad [23]$$

$$\Delta H = -0.23781 \text{ h}$$

The reaction of iodine with a cold alkaline environment gives hypoiodite and iodide according to the equation [22],

$$I_2 + 2\,OH^- \rightarrow H_2O + OI^- + I^- \qquad [24]$$

$$\Delta H = -0.56435 \text{ h}$$

It is expected that with evaporation of the water it would be driven entirely to completion giving concentrations of iodite and iodide. These are taken to be the prebiotic sources of iodine for these syntheses.

The total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for some of the 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
L-3,5,diiodo tyrosine (non-zwitterion)(23)	-14460.89603	0.18402
3,5,diiodo 4-hydroxy benzene$^+$(24)	-15323.49367	0.36619.
3-iodo-4-hydroxy benzene$^+$(25)	-8407.07042	0.38139
Mg.1,6-iodito-2,3,4,5-tetraen 7-yl octa-1-yl. porphin$^-$ (26)	-8482.01711	0.34996
Mg.1,5-iodo-6-one-2,3,4-trien 7-yl octa-1-yl. porphin$^-$ (27)	-8482.10986	0.31533
Mg.1,5-iodo-6-hydroxy-2,3,5-trien 7-yl octa-1-yl. porphin (28)	-8482.62201	0.36966
Mg.1,5-iodo-6-hydroxy-3,5-dien- 7-yl octa-1-yl. porphin$^+$ (29)	-8482.95487	0.37828
Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethynyl-1-yl. porphin (30)	-15400.34646	0.38710
Mg.1,2-amino 2-(3,5-diiodo-4-hydroxyphenyl) ethen-1-yl.porphin (31)	-15456.68543	0.43212
Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) 1H aziridin-2-yl.porphin (32)	-15456.70021	0.43270
Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin (33)	-15456.75638	0.43155
3,5-diiodo-4-hydroxyphenyl ethanimine (34)	-14271.60900	0.14379
Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin.CO (35)	-15569.73861	0.44168
Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) methanyl aziridine-2-one-1-yl.porphin (36)	-15569.76982	0.44218
3,5-diidotyrosine$^-$ (37)	-14460.35353	0.17217

3.12 The overall stoichiometry for the formation of L-thyroxine and L-triiodothyronine .

Although Mg.porphin is here taken as the catalyst for the reactions, the overall stoichiometry to form these molecules may be expressed as the formation of 3,5-diiodotyrosine, 3,5-diiodo-4-hydroxy benzene cation, and 3-iodo-4-hydroxy benzene cation, where the cations are not free, but present as stable charge transfer adducts.

$$H\text{-}(C\equiv C)_4\text{-}H + HOI + HI + NH_3 + CO + H_2O \rightarrow C_9H_9NO_3I_2 \qquad [25]$$

(23) 3,5-diiodotyrosine

$$\Delta H = -0.33458 \text{ h}$$

$$H\text{-}(C\equiv C)_3\text{-}H + HOI + 2HI \rightarrow I^- + H_2 + C_6H_3OI_2^+ \qquad [26]$$

(24) 3,5-diiodo-4-hydroxy benzene$^+$

$$\Delta H = 0.08618 \text{ h}$$

$$H\text{-}(C\equiv C)_3\text{-}H + H_2O + HI + H^+ \rightarrow H_2 + C_6H_4OI^+ \qquad [27]$$

(25) 3-iodo-4-hydroxy benzene$^+$

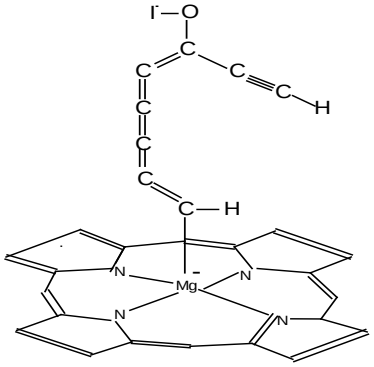
$$\Delta H = -0.36832 \text{ h}$$

The intermediates by which these stoichiometric reactions may have occurred are as follows:

3.13 The formation of Mg.1,6-iodito-2,3,4,5-tetraen 7-yl octa-1-yl. porphin$^-$ (26)

The Mg.H-(C ≡ C)$_4$-H.porphin in the triplet state should also be liable to nucleophilic attack by iodite, as shown,

Mg. H-(C≡C)$_4$-H .porphin + OI^{-1} →
(singlet)(12)



Mg.1,6-iodito-2,3,4,5-tetraen 7-yl octa-1-yl. porphin$^-$ (26) [28]

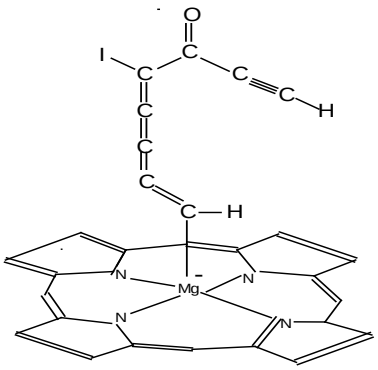
$\Delta H = -0.05891$ h

No activation energy was found for this addition.

3.14 The formation of Mg.1,5-iodo-6-one-2,3,4-trien 7-yl octa-1-yl. porphin$^-$

The Mg.1,6-iodito-2,3,4,5-tetraen 7-yl octa-1-yl. porphin$^-$ easily rearranges to give Mg.1,5-iodo-6-one-2,3,4-trien 7-yl octa-1-yl. porphin$^-$.

Mg.1,6-iodito-2,3,4,5-tetraen 7-yl octa-1-yl. porphin$^-$ →



Mg.1,5-iodo-6-one-2,3,4-trien 7-yl octa-1-yl. porphin$^-$ (27) [29]

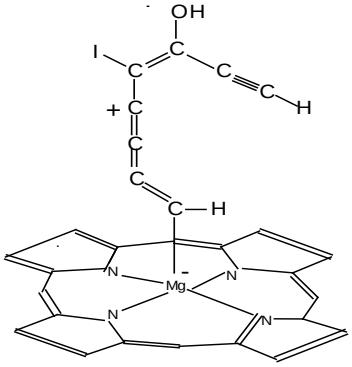
$\Delta H = -0.08889$ h

The activation energy to effect the rearrangement was 0.048 h, whilst the reverse required 0.155 h.

3.15 The formation of Mg.1,5-iodo-6-hydroxy-2,3,5-trien 7-yl octa-1-yl. porphin

The Mg.1,5-iodo-6-one-2,3,4-trien 7-yl octa-1-yl. porphin$^-$ easily picks up a proton to give the neutral, Mg.1,5-iodo-6-hydroxy-2,3,5-trien 7-yl octa-1-yl. porphin

Mg.1,5-iodo-6-one-2,3,5-trien 7-yl octa-1-yl. porphin$^-$ + H^+ →



Mg.1,5-iodo-6-hydroxy-2,3,5-trien 7-yl octa-1-yl. porphin (28) [27]

$\Delta H = -0.49848$ h

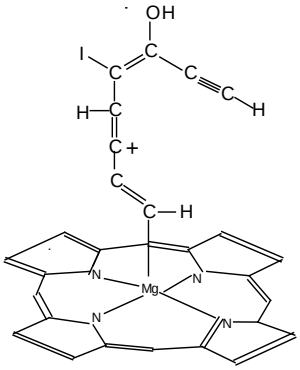
No activation energy was found for this addition.

These latter two reactions are equivalent to the addition of hypoiodous acid across the double bond.

3.16 The formation of Mg.1,5-iodo-6-hydroxy-3,5-dien 7-yl octa-1-yl. porphin

The Mg.1,5-iodo-6-hydroxy-2,3,5-trien 7-yl octa-1-yl. porphin may further protonate to give Mg.1,5-iodo-6-hydroxy-3,5-dien 7-yl octa-1-yl. porphin

Mg.1,5-iodo-6-hydroxy-2,3,5-trien 7-yl octa-1-yl. porphin + H^+ →



Mg.1,5-iodo-6-hydroxy-3,5-dien- 7-yl octa-1-yl. porphin $^+$ (29) [31]

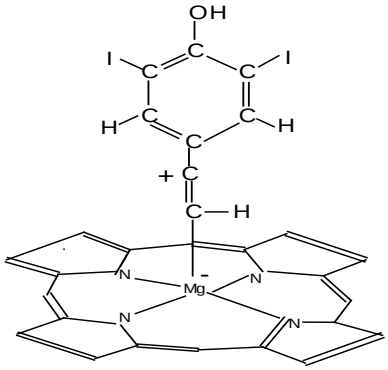
$\Delta H = -0.32518$ h

No activation was found for the protonation.

3.17 The formation of Mg.1,2-(3,5-diiodo-4-hydroxyphenyl)-ethynyl-1-yl. porphin

The Mg.1,5-iodo-6-hydroxy-3,5-dien 7-yl octa-1-yl. porphin may easily be attacked by the strong nucleophile, iodide anion, [23] to close the ring.

Mg.1,5-iodo-6-hydroxy-3,5-dien 7-yl octa-1-yl. porphin + I^- →



Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethynyl-1-yl. porphin (30) [32]

$\Delta H = -0.33442$ h

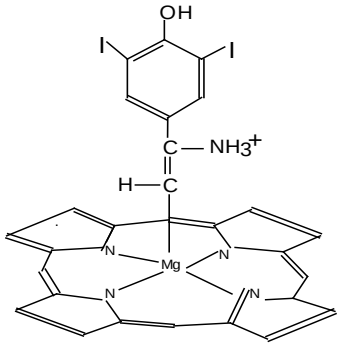
The activation energy to close the ring was 0.071 h.

The remaining steps in the synthesis exactly follow that for the formation of L-tyrosine except for the presence of the 3,5-diiodo substitution on the tyrosine ring.

3.18 The formation of Mg.1,2-amino 2-(3,5-diiodo-4-hydroxyphenyl) ethen-1-yl.porphin

The ammoniation is as,

Mg.1,2-(3,5-diiodo-4-hydroxyphenyl)-ethynl-1-yl. porphin + NH_3 →



Mg.1,2-amino 2-(3,5-diiodo-4-hydroxyphenyl) ethen-1-yl. porphin (31) [33]

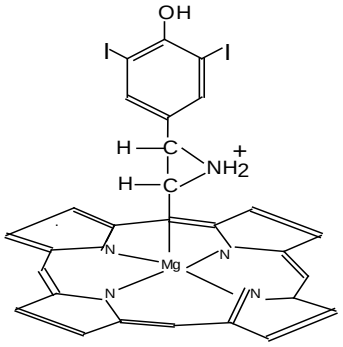
$\Delta H = 0.02240$ h

The activation energy was calculated as 0.032 h, whilst the dissociation required 0.010 h.

3.19 The formation of Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) 1H aziridin-2-yl.porphin

The Mg.1,2-amino 2-(3,5-diiodo-4-hydroxyphenyl) ethen-1-yl.porphin may cyclise during being activated to transfer a hydrogen atom.

Mg.1,2-amino 2-(3,5-diiodo-4-hydroxyphenyl) ethen-1-yl.porphin →



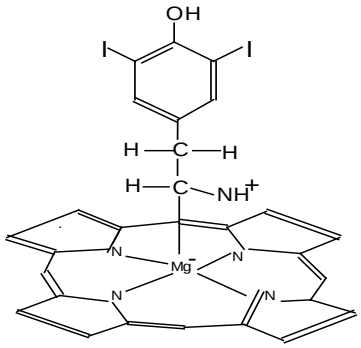
Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) 1H aziridin-2-yl. porphin (32) [34]

$\Delta H = -0.01427$ h

This ring closure occurs spontaneously during the optimization. The activation energy to form the carbon-hydrogen bond was 0.054 h, whilst the reverse was 0.051 h.

3.20 The formation of Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin

Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) 1H aziridin-2-yl.porphin →



Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin (33)

$\Delta H = -0.05720$ h

The activation energy to open the ring was calculated as 0.116 h, whilst that to close it was 0.175 h.

This adduct does require to be excited to release the 3,5-diiodo-4-hydroxy phenyl ethanimine,

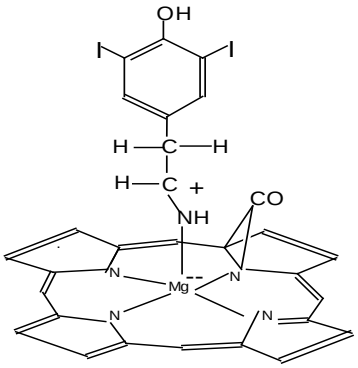
Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin → Mg.porphin + 3,5-diiodo-4-hydroxyphenyl ethanimine, (34) [36]

$\Delta H = 0.02922$ h

3.21 The formation of Mg.1,2-(3,5-diiodo-4-

hydroxyphenyl) ethanimin-1-yl.porphin.CO

Mg.porphin.CO + 3,5-diiodo-4-hydroxy phenyl ethanimine →

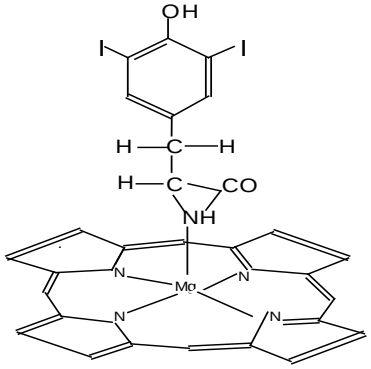


Mg.1,2-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin.CO (35) [37]

$\Delta H = -0.19752$ h

3.22 The formation of Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) methanyl aziridine-2-one-1-yl.porphin.

Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) ethanimin-1-yl.porphin.CO →



Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) methanyl aziridine-2-one-1-yl.porphin (36)

$\Delta H = -0.03176$ h

The activation energy to form the aziridone ring was 0.103 h, whilst the activation energy to open the ring was 0.160.

3.23 The formation L-3,5-diodotyrosine.

Hydrolysis of the Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) methanyl aziridine-2-one-1-yl.porphin.is depicted to yield the non-zwitterion form of L-3,4-diiodo tyrosine, as shown in Fig.3.

Mg.1,3-(3,5-diiodo-4-hydroxyphenyl) methanyl aziridine-2-one-1-yl.porphin. + H_2O → Mg.porphin +

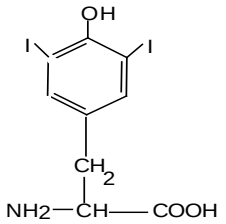


Fig.3. L-3,5-diidodotyrosine

$\Delta H = -0.04065$ h

Further ionisation may lead to the formation of the anion,

3,5-diiodotyrosine + OH^- → 3,5-diidotyrosine $^-$ + H_2O (37) [39]

$\Delta H = -0.13916$ h

and ultimately the zwitterion.

3.24 The formation 3,5-diiodo-4-hydroxy benzene cation,

The initial reactants are taken to be another acetylene derivative, triacetylene [9], iodite and iodide ion.

The total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for some of the stable molecules are given in Table 3.

Table 3

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

Molecule	MP2 hartree	ZPE (HF) hartree
triacetylene(38)	-228.92175	0.05261
Mg. H-(C ≡ C)$_3$-H .porphin (39) [21]	-1414.06685	0.33996
Mg.1,4-iodito-2,3-dien 5-yl hexa-1-yl.porphin$^-$ (40)	-8406.17968	0.34274
Mg.1,3-iodo-4-one 2,4,5-trien cyclohexan-1-yl.porphin$^-$ (41)	-8406.19806	0.34152
Mg.1,3-iodo-4-hydroxy 5-yl hexa-1-yl.porphin (42)	-8406.69718	0.38237
Mg.1,3,5-diiodo-4-hydroxy-benzen-1-yl. porphin (43)	-15324.43776	0.37763
Mg.3,5-diiodo-4-hydroxy benzen-1-yl.porphin cation (44)	-15323.49367	0.36619
3,5-diidodo-4-hydroxy benzene cation (45)	-14138.29744	0.07383
L-thyroxine (46)	-28598.99416	0.25350
iodite	-6991.96244	0.00118

iodide	-6917.05644	
hydrogen iodide	-6917.55229	0.00566
hypoiodous acid	-6992.55177	0.01362
iodine	-13834.19812	0.00057

3.25 The formation Mg.H-(C ≡ C)$_3$-H .porphin

The triacetylene forms a similar very weak van der Waals complex with the catalyst, Mg.porphin,

H-(C≡C)$_3$-H + Mg.porphin →

Mg. H-(C≡C)$_3$-H .porphin

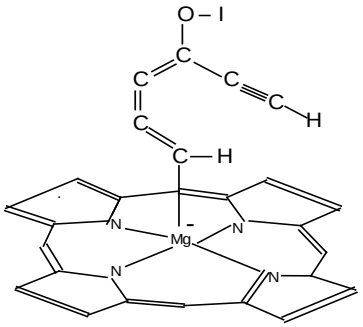
(38) (1) (39) [40]

ΔH = -0.02729 h

In the singlet state the adduct has a net positive charge of 0.03535 with positive charges on the adduct C4 and C5 of 0.177 and 0.320, respectively. It should be subject to nucleophilic attack by hydroxyl ion and iodite anions where the iodite anion is more electronegative on the oxygen atom. as shown,

Mg. H-(C≡C)$_3$-H .porphin + OI^{-1} →

(singlet)(39)



Mg.1,4-iodito-2,3-dien 5-yl hexa-1-yl.porphin$^-$

(40) [41]

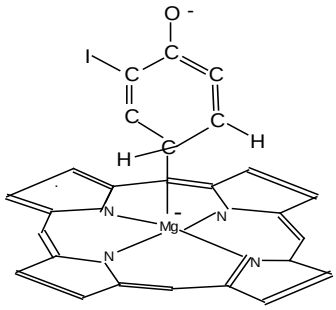
ΔH = -0.014897 h

No activation energy was recorded for this reaction.

3.26 The formation of Mg.1,3-iodo-4-one 2,3,5-trien cyclohexan-1-yl.porphin$^-$

The Mg.1,4-iodito-2,3,5-trien 5-yl hexa-1-yl.porphin may rearrange to Mg.1,3-iodo-4-one 2,3,5-trien cyclohexan-1-yl.porphin, as shown, and the ring close,

Mg.1,4-iodito-2,3-dien 5-yl hexa-1-yl.porphin →



Mg.1,3-iodo-4-one 2,4,5-trien cyclohexan-1-yl.porphin$^-$ (41)

[42]

ΔH = -0.01946 h

The reactant may also advantageously protonate before ring closure as,

Mg.1,3-iodo-4-one 5-yl hexa-1-yl.porphin + H^+ →

Mg.1,3-iodo-4-hydroxy 5-yl hexa-1-yl.porphin

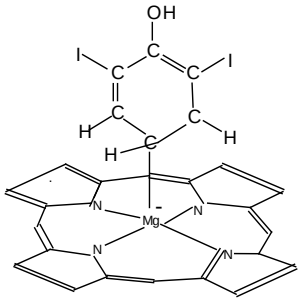
(42) [43]

ΔH = -0.52193 h

3.27 The formation of Mg.1,3,5-diiodo-4-hydroxy-benzen-1-yl. porphin$^-$

The Mg.1,3-iodo-4-one 2,4,5-trien cyclohexan-1-yl.porphin, may add the elements of hydrogen iodide as iodide is a strong nucleophile [23],

The Mg.1,3-iodo-4-hydroxy 2,4,5-trien cyclohexan-1-yl.porphin + HI →



Mg.1,3,5-diiodo-4-hydroxy-benzen-1-yl. porphin

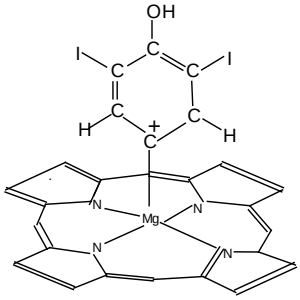
(43) [44]

ΔH = -0.13837 h

3.28 The formation Mg.1,3,5-diiodo-4-hydroxy benzen-1-yl.porphin cation,

The Mg.1,3,5-diiodo-4-hydroxy-benzen-1-yl. porphin may react with a proton to release hydrogen,

Mg.1,3,5-diiodo-4-hydroxy benzen-1-yl. porphin + H^+ → H_2 +



Mg.1,3,5-diiodo-4-hydroxy benzen-1-yl.porphin cation (44) [45]

$\Delta H = -0.20083$ h

This cation is stable with regard to its constituents,

Mg.3,5-diiodo-4-hydroxy benzen-1-yl.porphin$^+$ → Mg.porphin + 3,5-diiodo-4-hydroxy benzene$^+$ (45)

$\Delta H = 0.07398$ h

The adduct caries a small negative charge, -0.02.

3.29 The formation L-thyroxine

The 3,5-diodo-4-hydroxy tyrosine anion may react with the positively charged Mg.3,5-diiodo-4-hydroxy benzene-1-yl.porphin cation to give a neutral L-thyroxine as shown in Fig.4., with spontaneous release of the Mg.porphin catalyst.

L-3,5-diodotyrosine$^-$ + Mg.3,5-diiodo-4-hydroxy benzene.porphin$^+$ → Mg.porphin + [46]

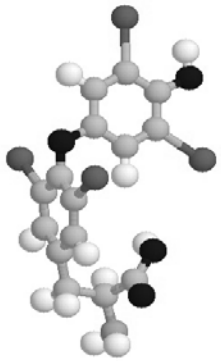


Fig.4. L-thyroxine (46)

$\Delta H = -0.26254$ h

No activation energy was recorded for this reaction .

3.30 The formation 3-iodo-4-hydroxy benzene cation.

The total energies and zero point energies for the HF and MP2/6-31G* equilibrium geometries for some of the stable molecules are given in Table 4.

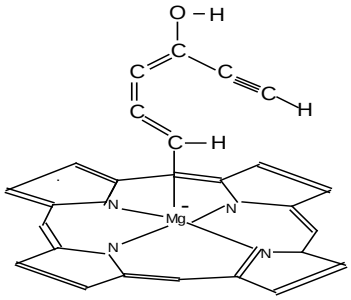
Table 4

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

Molecule	MP2 hartree	ZPE (HF) hartree
Mg.1,2,3-dien 4-hydroxy 5-yl hexa-1yl.porphin$^-$ (47)	-1489.71404	0.35377
Mg1,3-en 4-hydroxy 5-yl hexa-1yl.porphin (48)	-1490.28641	0.36957
Mg.1,4-hydroxy 2,3,5- trien cyclohexan-1-yl. porphin$^-$ (49)	-1489.75540	0.35424
Mg.1,3-iodo-4-hydroxy-benzen-1-yl. porphin (50)	-8408.01582	0.38919
Mg.3-iodo-4-hydroxy benzene-1-yl.porphin cation (51)	-8407.07042	0.381140
3-iodo-4-hydroxy benzene cation (52)	-7221.90774	0.08491
L-3,5,3'-triiodothyronine (53)	-21682.60165	0.26500

The Mg. H-(C ≡ C)$_3$-H .porphin adduct may also be subject to nucleophilic attack from hydroxyl anion,

Mg. H-(C≡C)$_3$-H .porphin + OH^{-1} → (singlet)(39)



Mg.1,2,3-dien 4-hydroxy 5-yl hexa-1yl.porphin$^-$ (47) [47]

$\Delta H = -0.12964$ h

No activation energy was recorded for this addition. The reaction is more energetic than for the addition of iodite, suggesting this may have given rise to ultimately more T3 than T4. The former being the more potent [1]. The adduct may protonate with a favourable energy change

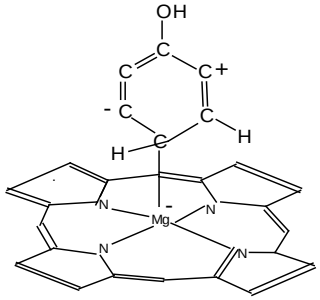
Mg.1,2,3-dien 4-hydroxy 5-yl hexa-1yl.porphin$^-$ + H^+ →

Mg.1,3-en 4-hydroxy 5-yl hexa-1yl.porphin (48) [48]

$\Delta H = -0.55831$ h

The adduct may also close with a favourable energy change without protonation,

Mg.1,2,3-dien 4-hydroxy 5-yl hexa-1yl.porphin →



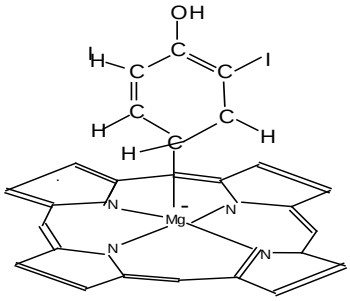
Mg.1,4-hydroxy 2,3,5- trien cyclohexan-1-yl. porphin$^-$
(49) [49]

$\Delta H = -0.04094$ h

3.31 The formation 3-iodo-4-hydroxy benzen-1-yl. porphin.

The Mg.1,4-hydroxy 2,3,5- trien cyclohexan-1-yl. porphin- may add a proton and iodide anion ,

Mg.1,4-hydroxy 2,3,5- trien cyclohexan-1-yl. porphin- + H^+ + HI →



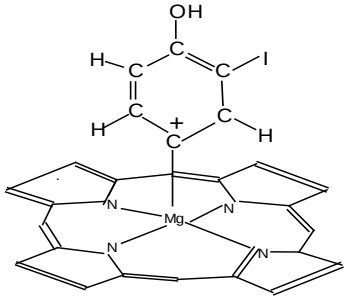
Mg.1,3-iodo-4-hydroxy-benzen-1-yl. porphin (50)
[50]

$\Delta H = -0.19212$ h

3.32 The formation Mg.3-iodo-4-hydroxy benzen-1-yl.porphin cation

Mg.1,3-iodo-4-hydroxy-benzen-1-yl.porphin may react with a proton to give a cation stabilized by the catalyst,

Mg.1,3-iodo-4-hydroxy-benzen-1-yl. porphin + H^+ → H_2 +



Mg.3-iodo-4-hydroxy benzen-1-yl.porphin cation
(51) [51]

$\Delta H = -0.17574$ h

This cation is stable with regard to its constituents,

Mg.3-iodo-4-hydroxy benzen-1-yl.porphin$^+$
→ Mg.porphin + 3-iodo-4-hydroxy benzene $^+$
(52) [52]

$\Delta H = 0.04366$ h

The adduct carries a charge of -0.45

3.33 The formation L-3,5,3'-triidothyronine (T3)

The 3,5-diodo-4-hydroxy tyrosine anion may react with the positively charged Mg.3-iodo-4-hydroxy benzene-1-yl.porphin cation to give a neutral L-3,5,3'-triidothyronine with spontaneous release of the Mg.porphin catalyst.

L-3,5-diodotyrosine$^-$ + Mg.3-iodo-4-hydroxy benzene-1-yl.porphin$^+$ →
L-3,5,3'-triidothyronine + Mg.porphin
(53) [53]

$\Delta H = -0.28967$ h

No activation energy was recorded for this reaction

4. Conclusion

Apart from the rate determining step involving the addition of ammonia to the alkyne [20-21], and ensuring a low rate of reaction, the remaining activation energies for the forward reactions have a lower, or comparable, value than the corresponding reverse reactions. Together with the achievable enthalpy changes these reactions do appear to be possible in a mildly reducing prebiotic atmosphere and should slowly, but spontaneously, produce some of these unique amino acids and be incorporated into proteins in molecular evolution to form important hormones. .. Further work at a higher accuracy may alter the values given here.

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