A Computational Study of a Prebiotic Synthesis of Ergosterol, Ergocalciferol & Cholecalciferol (Vitamin D2 and D3)

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Abstract: - The magnesium ion metalloporphyrin complex is shown to bind the ligands ethyne (e) and propyne (p) on the metal or nitrogen pyrrole sites as a two-site catalyst in their copolymerization. The order of addition of the monomers is (epep) to form the side-chain. The steroid ring D (pep) is formed first from the propyne adduct bound to the metal site and the nonane adduct bound to the N-site. The optimal orientation of these adducts determines the β-orientation of the 17-substituent. Further addition of three ethyne monomers forms an N-diene cyclopentene derivative able to cyclise to form the steroid ring C (pee) with a trans conformation and a 13-β methyl substituent. Further addition of propyne forms the B-ring (eep), followed by two ethyne to form the A-ring (pee). Reaction with a hydroxyl anion and a proton allows the catalyst to separate. Final hydrogenation renders ergosterol, photolysis leading to ergocalciferol (Vitamin D_2).
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, ergosterol, ergocalciferol (vitamin D_2), cholecalciferol (vitamin D_3), Mg.porphin

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1 Introduction

Ergosterol, (22E)-ergosta-5,7,22-trien-3β-ol), [1], [2], a yeast sterol, [3], Fig. 8, is converted by irradiation into ergocalciferol (Vitamin D_2), whilst 7-dehydrocholesterol, common in animal tissues is converted by radiation into cholecalciferol (Vitamin D_3). 7-dehydrocholesterol in the skin is the natural precursor of cholecalciferol in man, [3], whilst fish-liver oils are another source, [3]. Vitamin-D and its receptor (VDR), [4], participate in the regulatory machinery of gene control for skeletal development involving intestinal calcium and phosphate absorption, [5]. Dietary deficiency of vitamin D is regarded as the main causative factor for the development of rickets, [6]. Ergosterol is the form of vitamin D usually found in vitamin supplements, [7]. It is considered the first vitamin D analogue. The structural modifications from cholecalciferol reduce the affinity of ergocalciferol for the vitamin D binding protein resulting in faster clearance, limiting its activation, and altering its catabolism, [8].
Ergosterol regulates membrane fluidity and structure and is an important target for the activity of antifungals, [9].

These steroids are both derivatives of the saturated tetracyclic hydrocarbon, perhydrocyclopentane phenanthrene, [3]. This has six centres of asymmetry, [2], arising from the fusion of the four rings where the numbering and designation are standard, [1]. This steroid is closely related to the terpenes, [10], constructed of multiples of the five-carbon hydrocarbon isoprene (2-methyl-1,3-butadiene). The biosynthesis of ergosterol and cholesterol is from the steroid lanosterol, [11], [39], formed from the isoprene units of squalene (a dihydrotriterpene) consisting of consecutive isoprene units, [3].

From a prebiotic perspective, [12], it is desirable if the reactant molecules formed spontaneously from a supposed mildly reducing prebiotic atmosphere, [3], [13], whose constituents included hydrocarbon gases such as ethyne (e), propyne (p), carbon monoxide, ammonia, water, and hydrogen. Such an atmosphere has been shown to render possible and probable the formation of vitamins such as Vitamin B12, [14], thyroxine (T3 and T4), [15], hormones such as progesterone, [16], [40], stereospecific amino acids, [17], and lipoic acid. Critical to these prebiotic syntheses was the catalyst Mg.porphin, able to activate diverse reactions between weakly bonded charge transfer adducts on its surface to form classes of biological molecules such as D-sugars, L-amino acids, and terpenes, [18], [19].

This paper proposes a model for the catalytic photochemically activated copolymerization of these gases to form ergosterol where the order of polymerization is (epepepeeepee) on the catalyst magnesium porphin, and involves some hydroxylation and hydrogenation. The ergosterol may under photolysis give Vitamin D_2.

The prebiotic synthesis of cholecalciferol is very similar and both closely follow that of the prebiotic synthesis of the steroid hormone progesterone, [16], [40].

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 the steroid ergosterol 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 GAUSSIAN09, [20].

The standard calculations at the HF and MP2 levels including zero-point energy corrections are as previously published, [12].

3 Problem Solution

3.1 Total Energies (hartrees)

The steroid is described as being formed as a copolymerzation of the gases ethyne and propyne on the two site catalyst Mg.porphin. References prefaced by steroid refer to the standard steroid numbering as shown, in Fig. 1, [1].

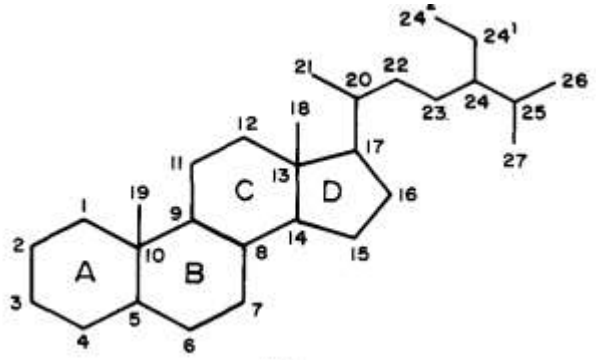


Fig. 1: Standard steroid substituent numbering, [1].

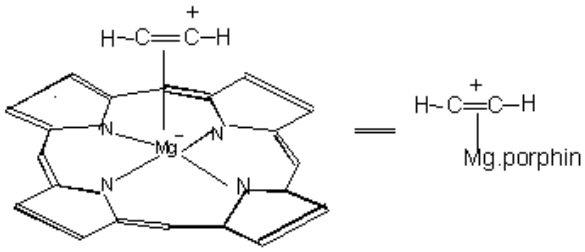
The gas ethyne may form two adducts with the catalyst on the metal and N-pyrrole sites, as follows.

The enthalpy of formation of the van der Waals complex is small but it appears stable.

Mg.porphin is a powerful catalyst able to form charge transfer complexes with a number of different kinds of molecules, [21], [22]. With ethyne, the ligand is positively charged (0.08) and the porphin has a negative charge, The acetylene sets as a ligand with a linear H-C ≡ C-H structure as shown.

Mg.1,porphin + H-C ≡ C- H →

(1)

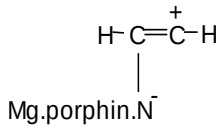


Mg.1, ethynyl.porphin

$$\Delta H = -0.01421 \text{ h}$$

The Mg.ethynyl.porphin may be photochemically excited for the ethyne to migrate to bond with a pyrrole unit as a higher energy ethyne adduct, [18], as shown,

Mg.1, ethynyl.porphin →



Mg.1, porphin.ethynyl (2)

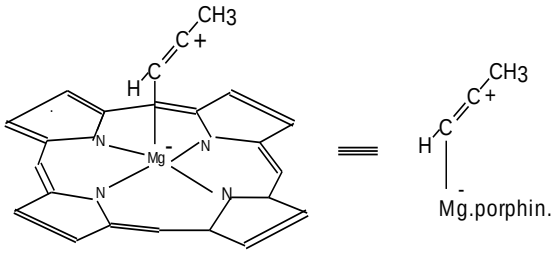
$$\Delta H = 0.01353 \text{ h}$$

The charge on the adduct is 0.07.

The gas propyne may also form two adducts with the catalyst on the metal and N-pyrrole sites, as follows:

The enthalpy of formation of the van der Waals complex is small but it appears stable.

Mg.porphin + CH_3-C ≡ C- H →

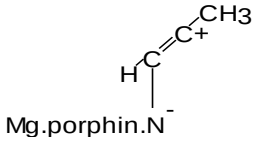


Mg.1,CH_3-C ≡ C- C-H.porphin (3)

ΔH = -0.00209 h

The charge on the propyne adduct is 0.07.

Mg.1, CH_3-C ≡ C-H.porphin →



(4)

Mg.1, porphin. CH_3-C ≡ C-H

ΔH = 0.01862 h

The charge on the propyne adduct was 0.19.

The first of these complexes on the metal site is lower in energy than the corresponding complex on the N-pyrrole site.

These complexes are integral reactants in the proposed synthesis. The energies of the stable complexes are shown 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	-1185.12250	0.29262
ethyne	77.06679	0.02945
Mg.1, ethynyl.porphin	-1262.19985	0.31797
Mg.1, porphin.ethynyl	-1262.18547	0.31701
propyne	116.24181	0.06010
Mg.1,propynyl.porphin	-1301.36738	0.35382
Mg.1,porphin.propynyl	-1301.34810	0.35308
ergosterol	-1164.48771	0.70897
Mg.1,propynyl.porphin.ethynyl	-1378.46158	0.37965
Mg.1,4-dehydro-2-methyl-but-1,3-dien-1-yl.porphin	-1378.42864	0.38160
Mg.1,ethynyl.porphin.ethynyl.	-1339.27189	0.34802
Mg.1,1-(cyclopropen-N2-yl)-1-dehydro-methan-1-yl.porphin	-1339.26595	0.35414
Mg.1,1.dehydro-1-(dehydro-cyclopropan-N2-yl).methan-1-yl.porphin	-1339.21922	0.35564
Mg.1,1-cyclopropen-1-yl-1-dehydro- methan-1-yl.porphin 14	-1339.23762	0.35108
Mg.1,1-dehydro-1-(1-hydroxy cyclopropan-1-yl) methan-1-yl.porphin	-1415.59591	0.38333
Mg.1,1-dehydro-2-hydroxy 2-methyl propan 1-yl.porphin	-1416.69175	0.40656
Mg.1,porphin.4-dehydro-2-methyl-but-1,3-dien-N1-yl.	-1378.36221	0.38402
Mg.1,ethynyl.porphin.4-dehydro-2-methyl -but-1,3-dien-N1-yl.porphin	-1455.44951	0.41583
Mg.1, 4-methen 3-methyl pent-en-1-yl.porphin$^+$	-1457.16216	
Mg.1,4-dehydro-3-(1-didehydro methyl)-4-methyl pent-1-en-N5-yl. porphin	-1455.43205	0.40513
Mg.1,3,4-(1-didehydro methyl) pent-1-en-1-yl.porphin	-1455.33851	0.41918
Mg.1,porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl	-1455.41199	0.41406
Mg.1,propynyl.porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl	-1571.60474	0.47722
Mg.1, 5,6-(1-didehydro methyl)-2-methyl-hept-1,3-dien-1-yl.porphin	-1571.66259	0.47999
Mg.1,porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin	-1571.70604	0.48578
Mg.1,ethynyl. porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin	-1648.78982	0.50278
Mg.1, 7,8-(1-didehydromethyl)-4-methyl- nonan-1,3,5-trien-1-yl.porphin	-1648.95251	0.50523
Mg.1,porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N-1-yl	-1648.76310	0.51924
Mg.1,propynyl. porphin.7,8-(1-didehydromethyl-4-methyl-) nonan-1,3,5-trien-N-1-yl	-1764.82675	0.57920
Mg.1,7,8-(1-didehydromethyl)-2,4-dimethyl-3-(1-ethen-N2-yl) nonan-1,5-dien-1-yl.porphin.	-1764.69778	0.58448

(17β) Mg.1,2-dehydro-2-methyl -3-(1-dehydro-4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin
- 1764.82750 0.59997
(17α) Mg.1,2-dehydro-2-methyl -3-(1-dehydro-4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin
-1764.79592
Mg.1, 2-dehydro-2-methyl-3-(1-dehydro 4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin $^{+}$
-1765.36800
Mg.1, Mg.1, 2-dehydro-2-methyl-3-(4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin
-1766.18132
Mg.1, 2-dehydro -2-methyl-3-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin
-1768.82220 0.66696
Mg.1, 2-dehydro -2-methyl-3-(1,4-dimethyl 5-methenyl hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin -1767.49801
Mg.1,2-dehydro-2-methyl-3-(4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin^{+}
-1765.21596
Mg.1,2-dehydro -2-methyl-3-(1,5-dimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin
-1729.66662
Mg.1,2-dehydro -2-methyl-3-(1,5-dimethyl-hexan-1-yl) cyclopentan-4-en-1-yl).porphin
-1730.92352
Mg.1, porphin.2-dehydro-2-methyl-3-(1,4,5-trimethy-hex-2-en-1-yl) cyclopentan-4-en-1-yl).
-1768.79265 0.67055
Mg.1,ethynyl porphin.2-dehydro-2-methyl-3-(1,4,5- trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl -1845.76098 0.69318
Mg.1, 2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl) cyclopentan-3-en-1-yl) ethen-1-yl.porphin -1845.89422 0.70258
Mg.1,porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl) cyclopentan-3-en-1-yl) ethen-N1-yl -1845.87425 0.70534
Mg.1,ethenyl.porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl)) cyclopentan-3-en-1-yl) ethen-N1-yl.porphin
-1922.7980 0.73091
Mg.1, 4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-1-yl.porphin -1922.90934 0.73634
Mg.1,porphin.4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-2-dehydro-3-en-1-yl) but-1,3-dien-N1-yl
-1923.00859 0.73989
Mg.1,ethynyl.porphin.4-(2-dehydro -1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-2-dehydro-3-en-1-yl) but-1,3-dien-N1-yl.porphin
-1999.92482 0.76664
Mg.1,6-(2-dehydro-1-methyl-5-(1,4,5-trimethy-hex-2-en-1-yl)) cyclopentan 3-en-1-yl) hex-1,3,5-trien 1-yl.porphin
-2000.07222 0.769834
Mg.1,6-(2-dehydro 5-isopropyl-1-methyl cyclopentan-3-en-1yl) hex-1,3,5-trien-1-yl.porphin (truncated) -1766.26913 0.61111
Mg.1,porphin,6-(2-dehydro 5-isopropyl -1-methyl cyclopent-3-en-1yl) hex-1,3,5-trien-N1-yl.
-1766.31937 0.61841
Mg.1,porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl)-ethen-N1-yl
-1766.44426 0.61390
Mg.1,propynyl.porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl)-ethen-N1-yl
-1882.84782 0.68302
Mg.1,2-(9H-4-ethen-N2-yl-1-isopropyl-8-methyl inden-5-yl)-propen-1-yl.porphin
-1882.84971 0.68687
Mg.1,des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.porphin
-1882.91182 0.68680
Mg.1,porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl
-1882.88921 0.69071
Mg.1,ethynyl. porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-N5-yl
-1959.98570 0.71770
Mg.1,2-(des-A-6,7,11,12,15,16-hexa-dehydro-pregnan-10-yl) ethen-1-yl.porphin
-1960.01249 0.71715
Mg.1,porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-N1-yl
-1960.04657 0.72534
Mg.1,ethynyl.porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-N1-yl -2037.04661 0.76347
Mg.1,4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-1-yl.porphin
-2037.14599 0.72348
Mg.1,porphin.4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-N4-yl. -2037.20007 0.76077
Mg.1,porphin 1,2,3,6,7,11,12,15,16-nonan-dehydro-20-methyl pregnan-4-yl
-2037.18750 0.76422
Mg.1,porphin.3-hydroxy-20-methyl-1,2,6,7,11,12,15,16-octa-dehydro pregnan-N4-yl)$^{-}$.
-2112.85520 0.78605
Mg.1,porphin. 2,3,6,7,11,12,15,16-octa-dehydro-1-hydroxy-20-methyl pregnan-N4-yl)$^{-}$

	-2112.77831	
Mg.1,porphin. 2,6,7,11,12,15,16-heptan-dehydro-1,3-dihydroxy-20-methyl pregnan-N4-yl)		
	-2188.26611	
Mg.1,porphin. 1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-N4-yl).porphin$^-$	2111.68173	0.75984
1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnane	-927.20068	0.48106
1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-ergostane	-1161.00427	0.63789
3-hydroxy ergostane	-1164.52497	0.70995
1,2,10,11,15,16-hexa dehydro ercalciol	-927.15954	0.47842
$OH^{\cdot}$	-75.52257	0.00911
OH^-	-75.51314	0.00885
H_2O	-76.19685	0.02298
H_2	-1.14414	0.01059

3.2 The Overall Stoichiometry for the Formation of the Steroid: Ergosterol (D, C, B, and A Rings).

Although Mg.porphin is here taken as the catalyst for the reaction, the overall stoichiometry to form the ergosterol (D, C, B, and A rings) is as follows,

$$8\ H\text{-}C \equiv C\text{-}H + 4\ CH_3\text{-}C \equiv C\text{-}H + H_2O + 5\ H_2 \rightarrow C_{28}H_{44}O$$

see Fig. 8: (ergosterol) (5)

$$\Delta H = -0.96534\ h$$

The enthalpy change is negative indicating that this may be the energetically favourable route to the initial formation of the steroid. The intermediates by which these stoichiometric reactions may have occurred are as follows where the first sequence involves the formation of the D-ring and substituents to close the C ring.

$$Mg.porphin + 3\ CH_3\text{-}C \equiv C\text{-}H + 6\ H\text{-}C \equiv C\text{-}H + 6H^{\cdot} \rightarrow Mg.C_{21}H_{30}.porphin \quad (6)$$

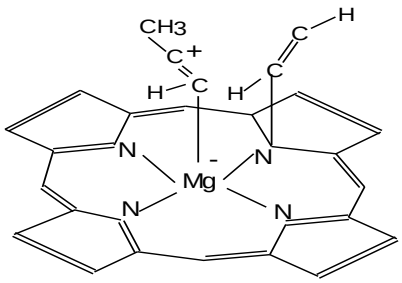
$$\Delta H = -0.31173\ h$$

The first sequence of reactions is as follows:
where the side-chain is placed in an extended conformation approaching that of the absolute configuration of the final product, ergosterol, Fig. 8. Hydrogenation of intermediates is largely left to the later stages of the sequence mechanism to allow the molecule to show its range of reactivity and feasible products. For clarity, the steroid rings are formed consecutively, but this is not essential.
Subsections mention variations that may occur for the prebiotic synthesis of ergosterol and cholecalciferol (Vitamin D_3) and its metabolic products, 25-hydroxycholecalciferol, and 1,25-dihydroxy-cholecalciferol, [3]. Chemical equations are numbered consecutively.

3.3 The Formation of Mg.1,propynyl. porphin.ethynyl.

With a vacant magnesium coordination site propyne may form a weak charge transfer complex with Mg.1,porphin.ethynyl as,

Mg.1,porphin.ethynyl + CH_3-C ≡ C- H



Mg.1,propynyl.porphin.ethynyl (7)

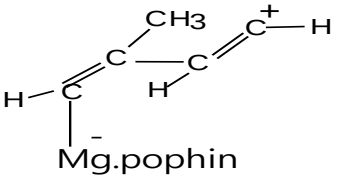
$$\Delta H = -0.03204\ h$$

The addition reaction is favourable and the adduct charges are: ethyne, 0.016, propyne 0.089.

3.4 The Formation of Mg.1, 4-dehydro-2-methyl-but-1,3-dien-1-yl.porphin

The Mg.1,propynyl.porphin.ethynyl adducts may coalesce to form a stable complex where some activation energy is required, as

Mg.1,propynyl.porphin.ethynyl →



Mg.1,4-dehydro-2-methyl-but-1,3-dien-1-yl.porphin (8)

$$\Delta H = 0.03467\ h$$

The charge on the adduct is 0.165.

At HF accuracy the form of the potential energy surface showing the excitation required is given in Fig. 2.

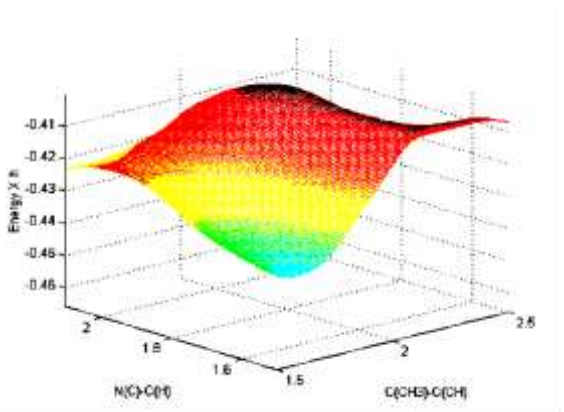


Fig. 2. The potential energy diagram for the formation of Mg.1,4-dehydro-2-methyl-but-1,3-dien-1-yl.porphin where the x-axis is $C(CH_3)$ – C(CH) and the y-axis the N(C)-C(H) bond extension. The Mg.1,propynyl.porphin.ethynyl is at (2.5,1.5), the bidentate chelate at (1.5,1.5), the Mg.1,4-dehydro-2-methyl-but-1,3-dien-1-yl.porphin at (1.5,2.5), the saddle point at (1.7,2.1). The energy = -1374 + X h.

Fig. 2, is similar to that for the formation of Mg.1,4-dehydro-pent-1,3-dien-1yl.porphin, [16], [40].
The activation energy to form the adduct was 0.128 h, and to dissociate it was 0.114 h. The enthalpy changes at HF accuracy being.

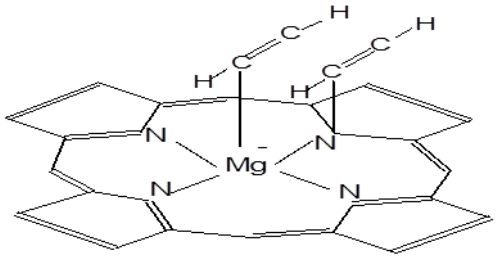
$$\Delta H = 0.013 \text{ h}$$

3.4.1 The Formation of Mg.1,2-hydroxy-2-methyl propanyl.porphin.

The synthesis of cholecalciferol (Vitamin D_3) has one less carbon in the side chain, suggesting it is initially formed by the polymerization on the catalyst of two ethyne molecules rather than the ethyne and propyne required for the formation of ergocalciferol (Vitamin D_2). The following set of reactions postulates how the side chains of cholecalciferol and 1,25-dihydroxy-cholecalciferol were originally formed as a variation to the ergocalciferol synthesis.

3.4.2 The Formation of Mg.1,ethynyl. porphin.ethynyl.

2 H-C ≡ C-H + Mg.porphin →

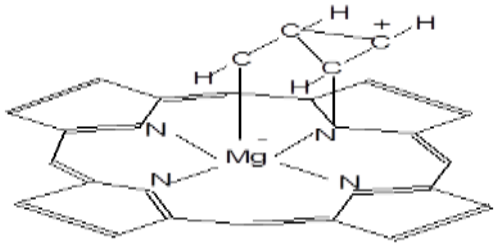


Mg.1,ethynyl.porphin.ethynyl (9)

$$\Delta H = -0.01893 \text{ h}$$

3.4.3 The Formation of Mg.1, 1-(cyclopropen-N2-yl)-1-dehydro-methan-1-yl.porphin

Mg.ethynyl.porphin.ethynyl →



Mg.1, 1-(cyclopropen-N2-yl)-1-dehydro-methan-1-yl.porphin (10)

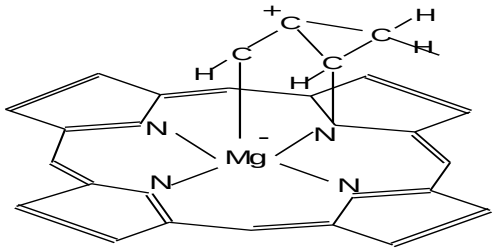
$$\Delta H = 0.01139 \text{ h}$$

Hydrogenation at this point in the synthesis would give the characteristic side-chain end grouping of cholecalciferol, $-CH_2-CH(CH_3)_2$.

3.4.4. The Formation of Mg.1,1.dehydro-1-(dehydro-cyclopropan-N2-yl).methan-1yl.porphin

This reaction involves a prototropic transfer as,

Mg.1, 1-cyclopropen-N2-yl-1-dehydro-methan-1-yl.porphin →



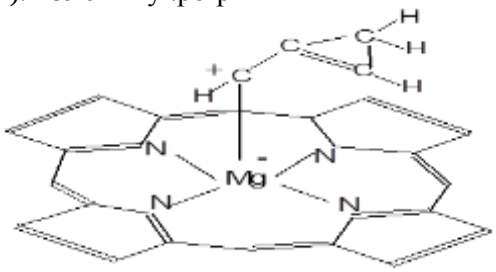
Mg.1,1.dehydro-1-(dehydro-cyclopropan-N2-yl).methan-1-yl.porphin (11)

$$\Delta H = 0.04806 \text{ h}$$

3.4.5. The Formation of Mg.1,1-dehydro-1-cyclopropen-1-yl methan-1-yl.porphin

This reaction involves a scission of the N-C bond on excitation as,

Mg.1,1.dehydro-1-(dehydro-cyclopropan-N2-yl).methan-1-yl.porphin →



Mg.1,1-cyclopropen-1-yl-1-dehydro- methan-1-yl.porphin (12)

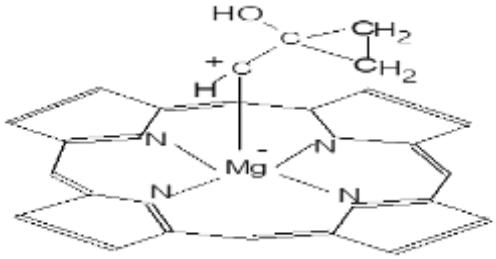
$$\Delta H = -0.02245\ h$$

At this point in the sequence, the adduct may be fully hydrogenated with molecular hydrogen, hydrogen ions such as the hydronium ion, or free radical hydrogen atoms to give the ultimate part of the D-ring side chain of cholecalciferol as, $-CH_2-CH(CH_3)_2$.

3.4.6 The Formation of Mg.1,1-dehydro-1-(1-hydroxy cyclopropan-1yl) methan-1-yl. porphin

This reaction involves the addition of the elements of water as,

H_2O + Mg.1, 1-cyclopropen-1-yl-1-dehydro-methan-1-yl.porphin
→



Mg.1,1-dehydro-1-(1-hydroxy cyclopropan-1-yl) methan-1-yl.porphin (13)

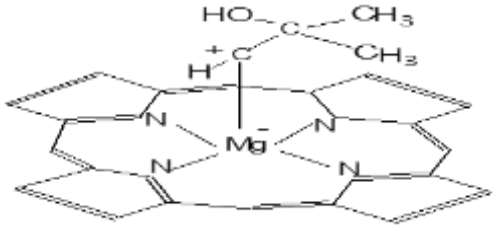
$$\Delta H = -0.14948\ h$$

This hydroxyl substituent occurs in the D-ring of 1,25-dihydroxy-cholecalciferol, the most active form of cholecalciferol, [3].

3.4.7 The Formation of Mg.1,1-dehydro-2-hydroxy-2-methyl propan-1-yl.porphin

This reaction is a facile hydrogenation on the strained cyclopropane ring as,

$2H\cdot$ + Mg.1,1-dehydro-(1-hydroxy cyclopropan-1-yl) methan-1-yl.porphin →



Mg.1,1-dehydro-2-hydroxy 2-methyl propan- 1-yl.porphin (14)

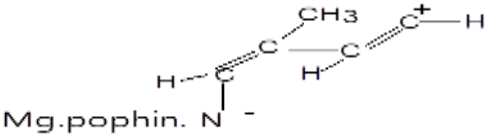
$$\Delta H = -0.07870\ h$$

The enthalpy of the reaction strongly suggests that it is facile with hydrogen free radicals rather than hydrogen molecules.
This substituent occurs in the D-ring of 1,25-dihydroxy-cholecalciferol.

3.5 The Formation of Mg.1,porphin.4-dehydro-2-methyl-but-1,3-dien-N1-yl

The Mg.1,4-dehydro-2-methyl-but-1,3-dien -1-yl.porphin may be excited by radiation to the higher energy state, as shown,

Mg.1, 4-dehydro-2-methyl -but-1,3-dien-1-yl.porphin →



Mg.1,porphin.4-dehydro-2-methyl-but-1,3-dien-N1-yl (15)

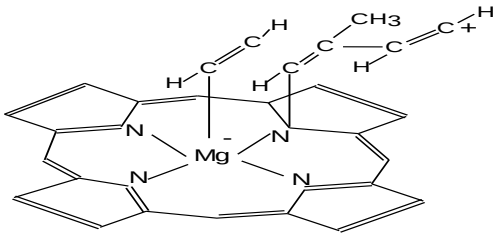
$$\Delta H = 0.06859\ h$$

The activation energy to form the adduct was the same as the enthalpy change. Adduct charge = -0.124.

3.6 The formation of Mg.1,ethynyl. porphin. 4-dehydro-2-methyl but-1,3-dien-N1-yl.porphin

Mg.1,porphin.4-dehydro-2-methyl -but-1,3-dien-N1-yl.porphin may add a further ethyne adduct on the free metal coordination site as,

H-C ≡ C-H + 4-dehydro-2-methyl-but-1,3-dien-N1-yl.porphin →



Mg.1,ethynyl.porphin.4-dehydro-2-methyl -but-1,3-dien-N1-yl.porphin (16)

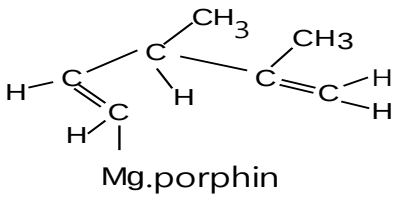
$$\Delta H = -0.01840 \text{ h}$$

Adduct charges were: ethyne, 0.0788, 4-dehydro-2-methyl but-1,3-dien-N1-yl, -0.142.

3.6.1 The Formation of Mg.1,3-methyl 4-methene pent-en-1-yl.porphin$^+$

The C2-C3 bond (1.474 Angstrom) of the Mg.1,ethynyl.porphin.4-dehydro-2-methyl -but-1,3-dien-N1-yl.porphin, (18), the adduct is slightly contracted suggesting some double bond character which might expose the di-radical able to react with molecular hydrogen without activation energy. The N-C bond is also liable to scission in the presence of a proton or other hydrogen species to give a highly exothermic reaction as,

Mg.1,ethynyl.porphin.4-dehydro-2-methyl -but-1,3-dien-1-yl.porphin + H_2 + H^+ →



Mg.1, 4-methen 3-methyl pent-en-1-yl.porphin$^+$ (17)

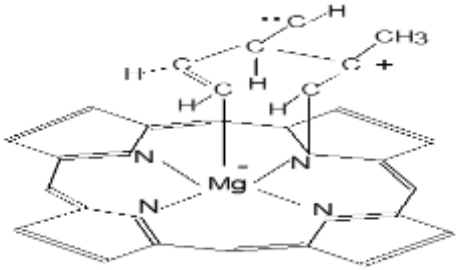
$$\Delta H_{(MP2)} = -0.67952 \text{ h}$$

However, as there are many favourable hydrogenation reactions, in this sequence of reactions hydrogenation is postponed until later to explore the reactivity of the adducts.

3.7 The Formation of Mg.1,4-dehydro-3-(1-didehydro methyl)-4-methyl pent-1-en-N5-yl. porphin.

The two adducts on Mg.1,ethynyl.porphin.4-dehydro-2-methyl -but-1,3-dien-1-yl.porphin, (18), may coalesce when excited to form a diradical, as,

Mg.1,ethynyl. porphin.4-dehydro-2-methyl but-1,3-dien-N1-yl.porphin →



Mg.1, 4-dehydro-3-(1-didehydro methyl)-4-methyl pent-1-en-N5-yl.porphin (18)

$$\Delta H = 0.00792 \text{ h}$$

Given the opposite charges on the adducts, they are expected to coalesce where the activation energy results from an in-plane electronic transition. The 24R was calculated as just 343 cal. below the 24S. The potential energy surface is given in Fig. 3.

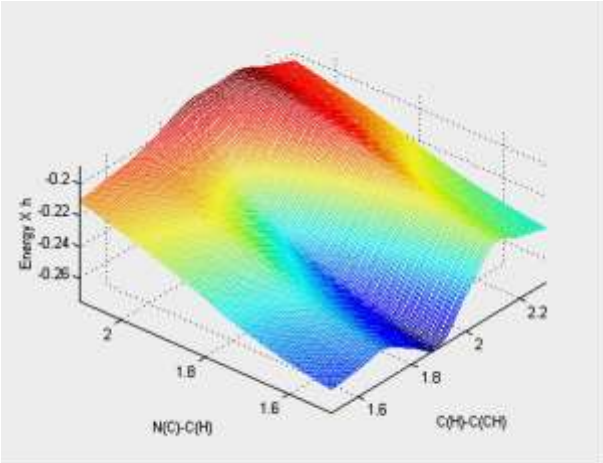


Fig. 3: The form of the potential energy surface for the bonding of the ethyne and 4-dehydro-2-methyl but-1,3-diene adducts on the surface of the catalyst Mg.porphin. The x-axis is the C(H)-C(CH) bond, and the y-axis is the N(C)-C(H) bond. The initial reactant is near (2.3,1.6), and the bonded product is at (1.9,1.5). The saddle point at (2.1,1.5). The N-C dissociated product at (1.5,2.2), The energy is -1451 + X h.

The form of the potential energy surface for the bonding is presented in Fig. 3. The activation energy to form the bond was 0.031 h whilst that to open it was 0.029 h. This is a bi-dentate chelate where the bond length is 1.9, between the normal single bond length of 1.54 and the dissociation limit of 2.1 Angstrom. The catalyst has its first excitation energy largely irrespective of surface adducts at 0.21 h. This is sufficient for the scission of the inter-adduct bond, the dissociation of the N-C bond, and the Mg-C bond. For this synthesis, it is assumed that only the N-C bond is dissociated rendering a greater entropy for the complex.

The enthalpy change at the HF level was,

$$\Delta H = 0.002 \text{ h}$$

The adduct charge was calculated as 0.199.

These di-adducts may give a preferred conformation as shown in Fig. 4.

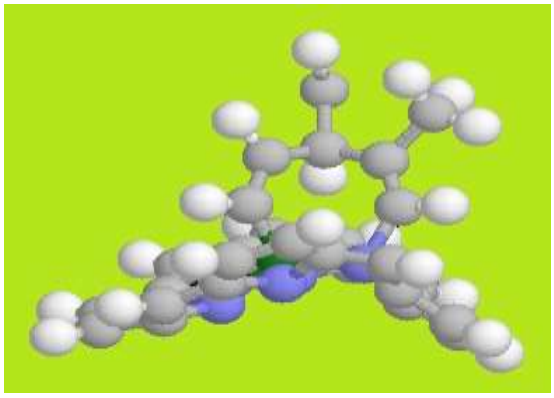


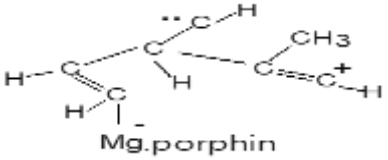
Fig. 4: The preferred conformation of Mg.1, 4-dehydro-3-(1-didehydro methyl)-4-methyl -pent-1-en-N5-yl.porphin

No extra bonding occurs between the nitrogen-bonded adduct C2 and the Mg-bonded adduct C2. This distance is never less than 2.5 Angstrom, well above the dissociation distance. It is this conformation which ultimately gives the configuration of the side chain, C24, in the final steroid structure, Fig. 11, as 24R or 24S.
The potential energy surface curve showing bonding of the C3 of the nitrogen-bound adduct at 1.9 Angstrom also suggests the facile formation of C2-C4 bonding giving Mg.1,ethynyl.porphin. 1-dehydro 2-(cyclopropenyl) where this would ultimately lead to the formation of the gem-dimethyl groups of the lanosterol group of steroids if three ethynes (eee) were initially added instead of epe, [23]. Two added propyne adducts may also give the characteristic gem-dimethyl groups, [19].

3.8 The Formation of Mg.1,3,4-(1-didehydro methyl) pent-1-en-1-yl.porphin

The Mg.1, 4-dehydro-3-(1-didehydro methyl) - 4-methyl pent-1-en-N5-yl. porphin is liable to dissociation from the N-pyrrole site with some activation energy as,

Mg.1, 4-dehydro -3-(1-didehydro methyl) -4-methyl pent-1-en-N5-yl. porphin →



Mg.1,3,4-(1-didehydro methyl) pent-1-en-1-yl.porphin (19)

$$\Delta H = 0.10605 \text{ h}$$

The activation energy for the C-N dissociation was calculated at HF as,

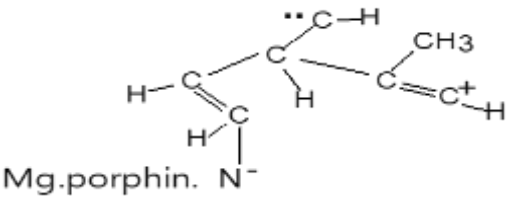
$$\Delta H = 0.06 \text{ h}$$

The charge on the adduct was -0.039.

3.9 The Formation of Mg.1,porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl

The Mg.1,3,4-(1-didehydro methyl) pent-1-en-1-yl.porphin may be excited to a higher energy state as,

Mg.1,3,4-(1-didehydro methyl pent-1-en-1-yl.porphin →



Mg.1,porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl (20)

$$\Delta H = -0.07803 \text{ h}$$

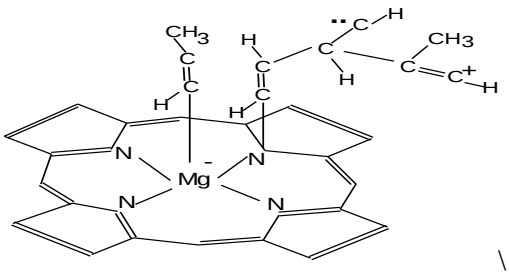
The activation energy was the same as the enthalpy change. The charge on the adduct was -0.441.

If required, this highly reactive adduct may be partially hydrogenated as it only requires the close proximity of a hydrogen molecule for a reaction to occur with the di-radical without activation energy in a strongly exothermic reaction.

3.10 The Formation of Mg.1,propynyl. porphin 3,4-(1-didehydro methyl) pent-1-en-N1-yl

The Mg.1,porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl may add a further propyne adduct on the vacant magnesium ion site as,

CH_3-C ≡ C-H + Mg.1,porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl →



Mg.1,propynyl.porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl (21)

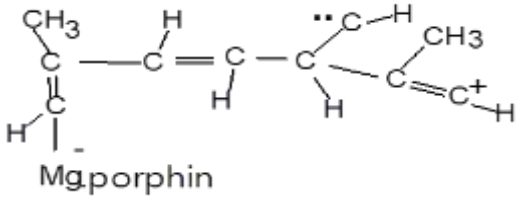
$$\Delta H = 0.05178 \text{ h}$$

No activation energy is required to form the charge transfer adduct. The charge on the adduct was propyne 0.354, N-adduct -0.477.

3.11 The Formation of Mg.1, 5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin.

The Mg.1,propynyl.porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl may be excited to coalesce to form a stable magnesium ion adduct as,

Mg.1,propynyl. porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl →



Mg.1, 5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin**.** (22)

$$\Delta H = -0.05539 \text{ h}$$

The potential energy surface for this bonding is shown in Fig. 5.

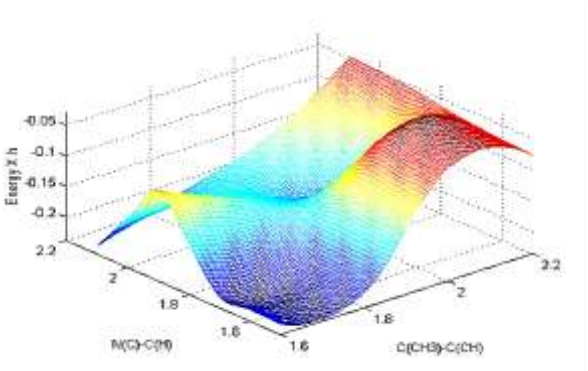


Fig. 5: The form of the potential energy surface for the bonding of the Mg.1,propynyl. porphin.3,4-(1-didehydro methyl) pent-1-en-N1-yl adducts on the surface of the catalyst Mg.porphin. The initial reactant is near (2.2,1.5), and the product is at (1.6,1.6). The N-C dissociated product at (1.6,2.2) The saddle point at (2.1,1.5) The energy is -1567 + X h.

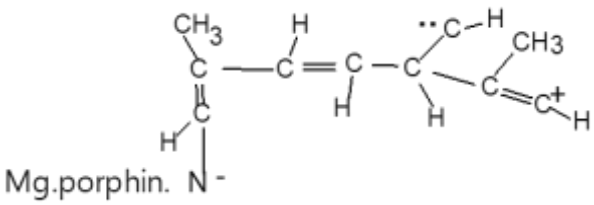
The activation energy for the transformation was found to be 0.071 h, whilst the activation energy for the reverse reaction was 0.107 h. The adduct charge was -0.475.

These charges may orient the adducts to bond as shown by the magnetic field of the radiation being perpendicular to the plane of the porphin and directed toward the observer. Steric effects are also determinants, [16], [40].

3.12 The Formation of Mg.1,porphin. 5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin

The Mg.1,5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin may be promoted to the higher energy N-bound state as,

Mg.1,5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin →



Mg.1,porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin (23)

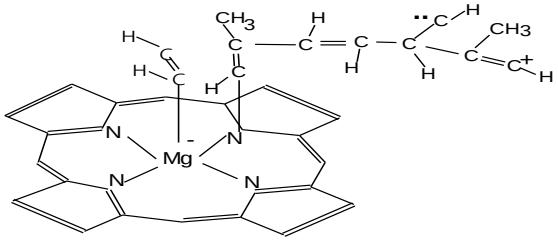
$$\Delta H = -0.03829 \text{ h}$$

The activation energy is the same as the enthalpy change.
The charge on the adduct was -0.396

3.13 The Formation of Mg.1,ethynyl. porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin.

Mg.1,porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin may accept a further ethyne adduct as,

H-C ≡ C-H + Mg.1,porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin →



Mg.1,ethynyl.porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin**.** (24)

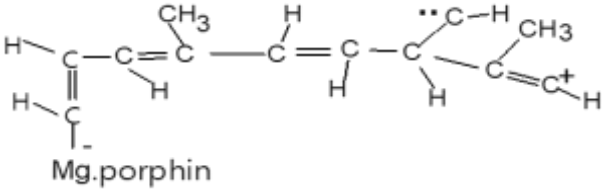
$$\Delta H = -0.02807 \text{ h}$$

The charge on the ethyne was -0.019, and the charge on the N-entity, -0.235.

3.14 The Formation of Mg.1,7,8-(1-didehydromethyl)-4-methylnonan-1,3,5-trien-1-yl.porphin

Ultraviolet light may cause coalescing of the adducts as,

Mg.1,ethynyl.porphin.5,6-(1-didehydro methyl)-2-methyl hept-1,3-dien-1-yl.porphin →



Mg.1,7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-1-yl.porphin (25)

$$\Delta H = -0.16051$$

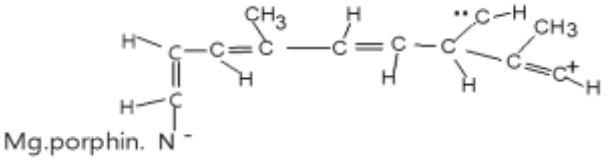
No activation energy was calculated to bond the two adducts.

The charge on the adduct was 0.289.

3.15 The Formation of Mg.1,porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N-1-yl

The Mg.1, 7, 8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-1-yl.porphin may be excited to a higher energy state as,

Mg.1,7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-1-yl.porphin.→



Mg.1,porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N-1-yl (26)

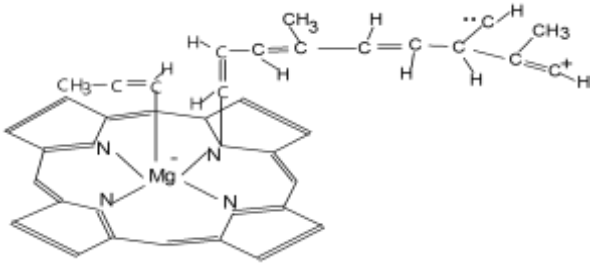
$$\Delta H = 0.20188 \text{ h}$$

The activation energy was the same as the enthalpy change. Adduct charge was -0.536

3.16 The Formation of Mg.1,propynyl. porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N1-yl

The Mg.1, porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N-1-yl may add a further propyne as,

CH_3-C ≡ C-H + Mg.1,porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N1-yl →



Mg.1,propynyl.porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N1-yl (27)

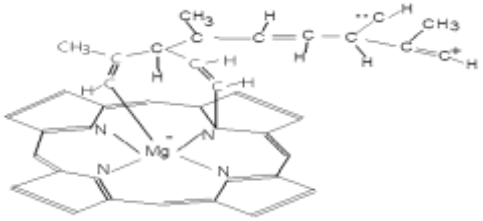
$$\Delta H = 0.17804 \text{ h}$$

The adducts charges were propyne 0.179, N-entity, -0.567.

3.17 The Formation of Mg.1,7,8-(1-didehydromethyl)-2,4-dimethyl-3-(1-ethen-N2-yl) nonan-1,5-dien-1yl. porphin.

It is shown that the two adducts may bond as,

Mg.1,propynyl.porphin.7,8-(1-didehydromethyl)-4-methyl nonan-1,3,5-trien-N1-yl →



Mg.1,7,8-(1-didehydromethyl)-2,4-dimethyl-3-(1-ethen-N2-yl) nonan-1,5-dien-1yl.porphin.

(28)

$$\Delta H = 0.14467 \text{ h}$$

The activation energy at the HF level for the forward reaction was 0.018 h and for the backward reaction 0.058 h.

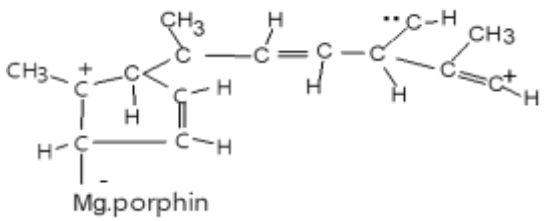
The adduct charge was -0.378.

In this bonding, an asymmetric C3 is formed with two stereoisomers possible that affect the energies of the subsequent cyclised cyclopentane derivatives. At this stage in the sequence of the mechanism, it is possible for the molecule in an excited state to cyclise and form the prospective D-ring of the steroid ergosterol.

3.18 The Formation of Mg.1,2-dehydro-2-methyl -3-(1-dehydro 4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin

The Mg.1,7,8-(1-didehydromethyl-2,4-dimethyl-3-(1-ethen-N2-yl)) nonan-1,5-dien-1yl.porphin. may cyclise with activation as shown,

Mg.1,7,8-di-(1-didehydromethyl)-2,4-dimethyl-3-(1-ethen-N2-yl) nonan-1,5-dien-1yl.porphin.→



Mg.1,2-dehydro-2-methyl-3-(1-dehydro-4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin (29)

$$\Delta H = -0.11594 \text{ h}$$

The activation energy to form the D-ring was 0.04 h, that for the reverse reaction 0.23 h.

The adduct charge was 0.020.

This 17β isomer was calculated as 0.032 h below that of the 17α isomer (32), establishing the symmetry of C17.

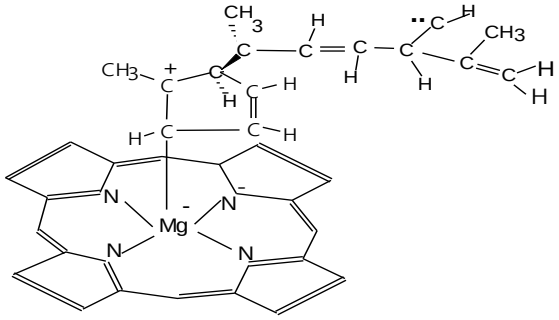
3.19 The Formation of Mg.1, 2-dehydro-2-methyl-3-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin

The Mg.1,2-dehydro-2-methyl -3-(1-dehydro-4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin may be progressively hydrogenated to possess a less reactive side-chain. Just two routes are suggested:

3.19.1 The Formation of Mg.1, 2-dehydro-2-methyl-3-(1-dehydro 4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin

The first involves protonation of side-chain C6 followed by reaction with molecular hydrogen, as,

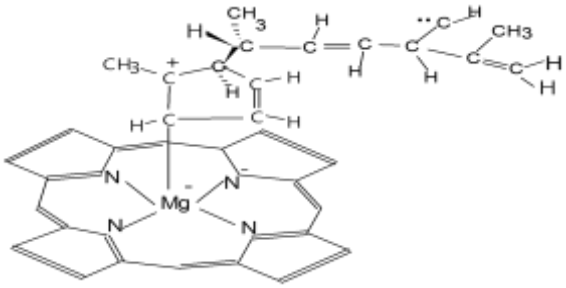
Mg.1,2-dehydro-2-methyl-3-(1-dehydro-4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porpnhin $+ H^+ \rightarrow$



Mg.1, 2-dehydro-2-methyl-3-(1-dehydro 4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin $^+$ (30)

$$\Delta H_{(MP2)} = -0.54050 \text{ h}$$

Mg.1, 2-dehydro-2-methyl-3-(1-dehydro-4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin$^+$ + $H_2 \rightarrow H^+$ +



Mg.1, Mg.1, 2-dehydro-2-methyl-3-(4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin (31)

$$\Delta H_{(MP2)} = 0.33082 \text{ h}$$

Mg.1, Mg.1, 2-dehydro-2-methyl-3-(4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin + $2H_2$ → Mg.1, 2-dehydro-2-methyl-3-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin (32)

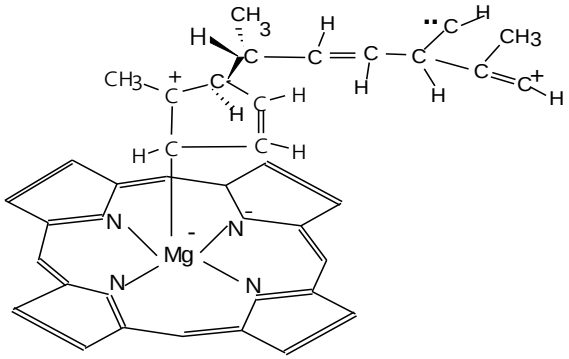
$$\Delta H_{(MP2)} = -0.35255 \text{ h}$$

Mg.1, 2-dehydro-2-methyl-3-(1,4-dimethyl-5-methenyl)-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin, is the intermediate.

3.19.2 The Formation of Mg.1,2-dehydro-2-methyl-3-(4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin$^+$

The second involves protonation of side-chain C1 followed by reaction with molecular hydrogen, as,

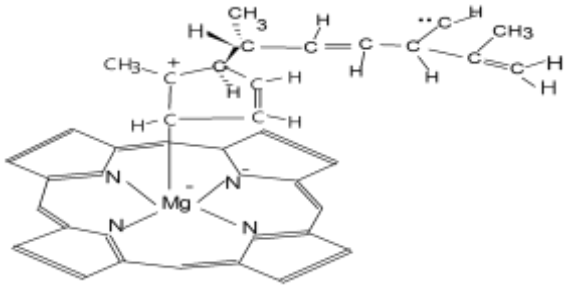
Mg.1,2-dehydro-2-methyl-3-(1-dehydro-4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porpnhin + H^+ →



Mg.1,2-dehydro-2-methyl-3-(4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin$^+$ (33)

$$\Delta H_{(MP2)} = -0.38846 \text{ h}$$

Mg.1,2-dehydro-2-methyl-3-(4,5-(1-didehydromethyl)-1-methyl hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin$^+$ + H_2 → H^+ +



Mg.1, 2-dehydro-2-methyl-3-(4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin (34)

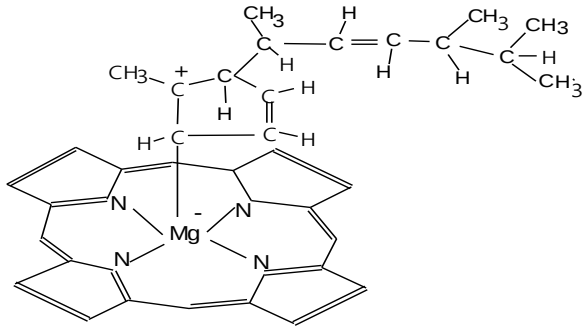
$$\Delta H_{(MP2)} = 0.17878 \text{ h}$$

Mg.1, Mg.1, 2-dehydro-2-methyl-3-(4-didehydro methyl 5-methenyl 1-methyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin + $2H_2$ → Mg.1, 2-dehydro-2-methyl-3-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin (35)

$$\Delta H_{(MP2)} = -0.35260 \text{ h}$$

These two routes to the fully hydrogenated side-chain may be summarized as,

Mg.1,2-dehydro-2-methyl -3-(1-dehydro -4,5-(1-didehydromethyl)-1-methyl -hex-2-en-1-yl) cyclopentan-4-en-1-yl.porphin + $3H_2$ →



Mg.1, 2-dehydro-2-methyl-3-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin (36)

$$\Delta H = -0.53091 \text{ h}$$

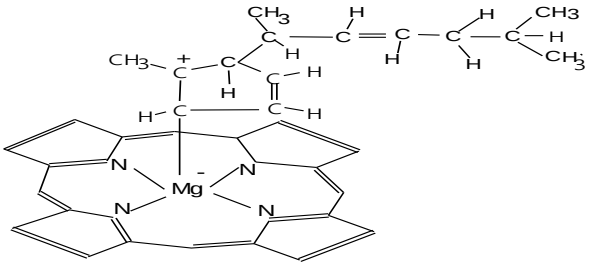
This sum of the reactions is exergonic with molecular hydrogen or hydrogen radicals and without activation energy.

The charge on the adduct was -0.331.

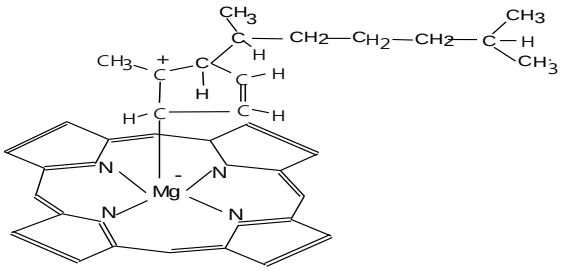
The 20S isomer was calculated to be 0.031 h below the 20R isomer establishing the asymmetry of C20.

3.19.3 The Formation of Mg.1, 2-dehydro -2-methyl-3-(1,5-dimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin

In the formation of cholecalciferol, the hydrogenation is presumed to go further displayed as,



Mg.1, 2-dehydro-2-methyl-3-(1,5-dimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin + H_2 →



Mg.1, 2-dehydro -2-methyl-3-(1,5,-dimethy-hexan-1-yl) cyclopentan-4-en-1-yl).porphin

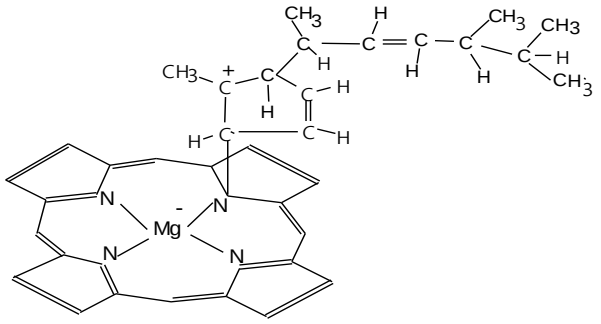
(37)

$$\Delta H_{(MP2)} = -0.11276 \text{ h}$$

3.20. The Formation of Mg.1, porphin.2-dehydro -2-methyl-3-(1,4,5-trimethy-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin

The Mg.1, 2-dehydro-2-methyl-3-(1,4,5-trimethy-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin may be excited to a higher energy state as,

Mg.1, 2-dehydro-2-methyl-3-(1,4,5,-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin →



Mg.1, porphin.2-dehydro-2-methyl-3-(1,4,5,-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl

(38)

$$\Delta H = 0.03274 \text{ h}$$

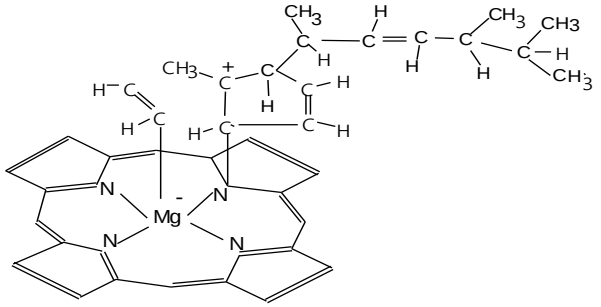
The activation energy is the same as the enthalpy change.

The charge on the adduct was -0.316.

3.21 The Formation of Mg.1,ethynyl porphin.2-dehydro -2-methyl-3-(1,4,5,-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl

A further ethyne molecule may add as an adduct on the magnesium ion site as,

Mg.1, porphin.2-dehydro-2-methyl-3-(1,4,5,-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl).porphin + ethyne →



Mg.1,ethynyl porphin.2-dehydro-2-methyl-3-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-4-en-1-yl

(39)

$$\Delta H = 0.09240 \text{ h}$$

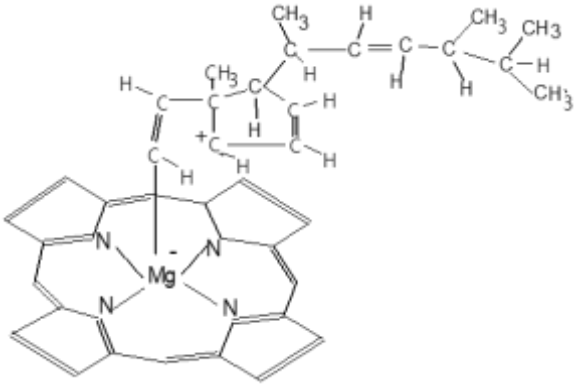
The activation energy to form the weakly bonded van der Waals complex is negligible.

The adduct charges were ethyne -0.225, N-entity -0.152.

3.22 The Formation Mg.1, 2-(2-dehydro -1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl) cyclopentan-3-en-1-yl) ethen-1-yl.porphin

The adducts may coalesce as,

Mg.1,ethynyl porphin.2-dehydro -2-methyl-3-(1,4,5-trimethy-hex-2-en-1-yl) cyclopentan-4-en-1-yl →



Mg.1, 2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl) cyclopentan-3-en-1-yl) ethen-1-yl.porphin (40)

$$\Delta H = -0.12489 \text{ h}$$

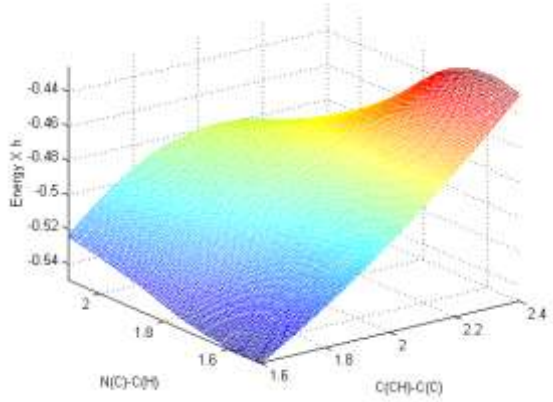


Fig. 6: The potential energy surface for the coalescing of Mg-ion and N-adducts on the catalyst Mg.porphin. The initial state is at coordinates (2.4,1,5). The product at (1.5,2.2). The saddle point at (2.1,2.2). The N-C un-dissociated product at (1.6,1.6). The energy is -1840 + X h.

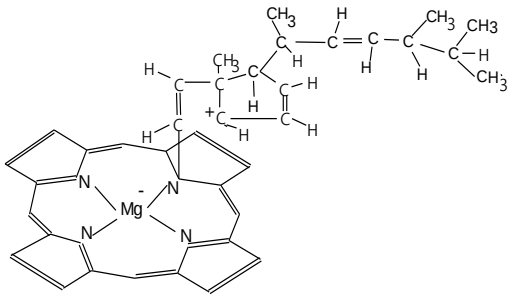
The potential energy surface for the coalescing is presented in Fig. 6. The activation energy at the HF level for the forward reaction was not found.

The adduct charge was 0.329.

3.23 The Formation of Mg.1,porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl).ethen-N1-yl.

The Mg.1, 2-(2-dehydro-1-methyl-5-(1,4,5-trimethy-hex-2-en-1yl) cyclopentan-3-en-1-yl).ethen-1-yl.porphin may be excited to a higher energy state as,

Mg.1, 2-(2-dehydro-1-methyl-5-(1,4,5-trimethy-hex-2-en-1yl) cyclopentan-3-en-1-yl).ethen-1-yl.porphin →



Mg.1,porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl) cyclopentan-3-en-1-yl) ethen-N1-yl. (41)

$$\Delta H = 0.02243 \text{ h}$$

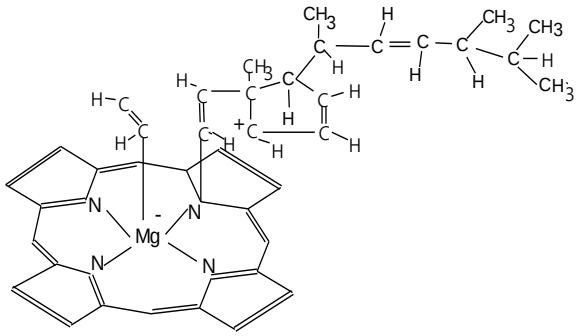
The activation energy being the same as the enthalpy change.

The adduct charge was -0.480.

3.24 The Formation of Mg.1,ethenyl. porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl)) cyclopentan-3-en-1-yl) ethen-N1-yl.porphin

The Mg.1,porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethy-hex-2-en-1yl) cyclopentan-3-en-1-yl).ethen-N1-yl may add a further adduct of ethyne on the vacant magnesium ion site as,

Mg.1,porphin.2-(2-dehydro-1-methyl-3-(1,4,5-trimethyl-hex-2-en-1yl) cyclopentan-3-en-1-yl) ethen-N1-yl + H-C ≡ C-H →



Mg.1,ethenyl.porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1yl)) cyclopentan-3-en-1-yl) ethen-N1-yl.porphin (42)

$$\Delta H = 0.14779 \text{ h}$$

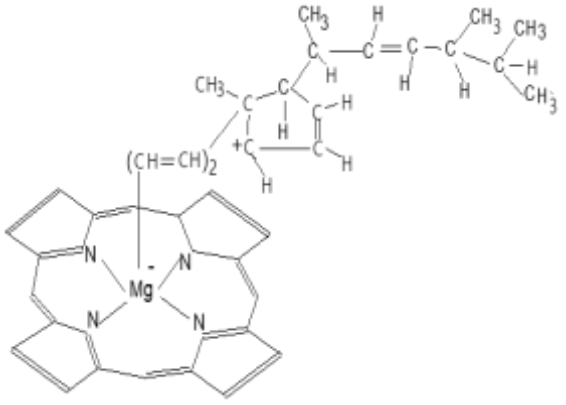
The activation energy is the same as the enthalpy change.

The charges on the ethyne and N-entity were 0.107 and -0.518, respectively.

3.25 The Formation of Mg.1,4-(2-dehydro -1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-1-yl.porphin

The adducts of Mg.1,ethenyl.porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethy-hex-2-en-1yl)) cyclopentan-3-en-1-yl) ethen-N1-yl.porphin may bond as,

Mg.1,ethenyl.porphin.2-(2-dehydro-1-methyl-5-(1,4,5-trimethy-hex-2-en-1yl)) cyclopentan-3-en-1-yl) ethen-N1-yl.porphin →



Mg.1, 4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-1-yl.porphin (43)

$$\Delta H = -0.11471 \text{ h}$$

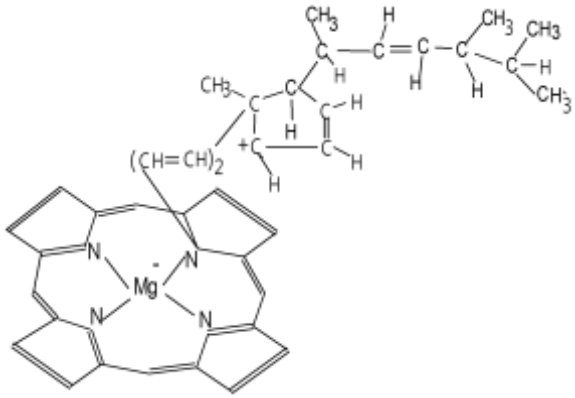
No activation energy was calculated for this bonding.

The charge on the adduct was 0.980.

3.26 The Formation of Mg.1,porphin.4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-N1-yl.

The Mg.1, 4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-1-yl.porphin also forms a high energy state on excitation as,

Mg.1,4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-1-yl.porphin →



Mg.1,porphin.4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-N1-yl (44)

$$\Delta H = -0.09609 \text{ h}$$

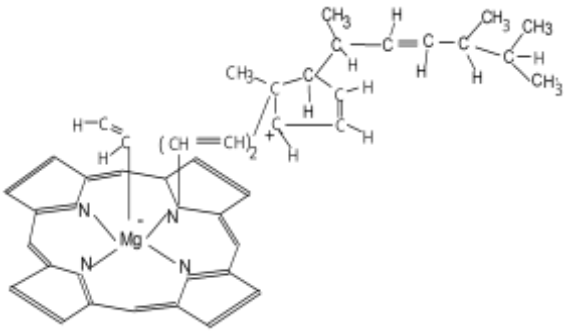
The activation energy is the same as the enthalpy change.

The charge on the adduct was -0.442.

3.27 The Formation of Mg.1,ethynyl. porphin.4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl)-N1-yl.porphin

A further molecule of ethyne may be added as,

Mg.1,porphin.4-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-1-yl + H-C ≡ C-H →



Mg.1,ethynyl.porphin.4-(2-dehydro -1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-N1-yl (45)

$$\Delta H = 0.14816 \text{ h}$$

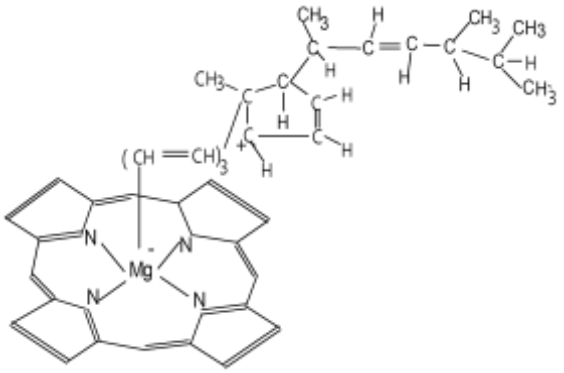
No activation energy was recorded for this addition.

The charge on the adduct was ethyne 0.063, N-entity -0.507.

3.28 The Formation of Mg.1,6-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl)) cyclopentan-3-en-1-yl) hex-1,3,5-trien 1-yl

The adducts may bond as,

Mg.1,ethynyl.porphin.4-(2-dehydro -1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl) cyclopentan-3-en-1-yl) but-1,3-dien-N1-yl . →



Mg.1,6-(2-dehydro-1-methyl-5-(1,4,5-trimethyl-hex-2-en-1-yl)) cyclopentan-3-en-1-yl) hex-1,3,5-trien 1-yl.porphin
. (46)

$$\Delta H = -0.14456 \text{ h}$$

No activation energy was recorded for this reaction.

The charge on the adduct was 0.161.

The sum of all reactions in the sequence mechanism may be expressed as,

Mg.porphin + 3 CH_3-C ≡ C-H + 6 H-C ≡ C-H + 6H· → Mg.$C_{21}H_{30}$.porphin

$$\Delta H = -0.31173 \text{ h}$$

At this point in the reaction sequence, the side chain was reduced in size to reduce computation time. It is subsequently assumed that the enthalpy changes would not be noticeably changed by the effective truncation of the side chain.

The revised structure of the molecule in an extended conformation is as depicted (Fig. 7),

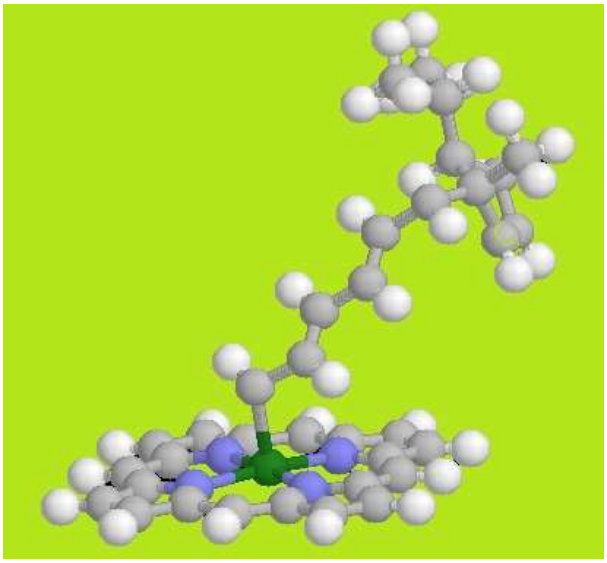


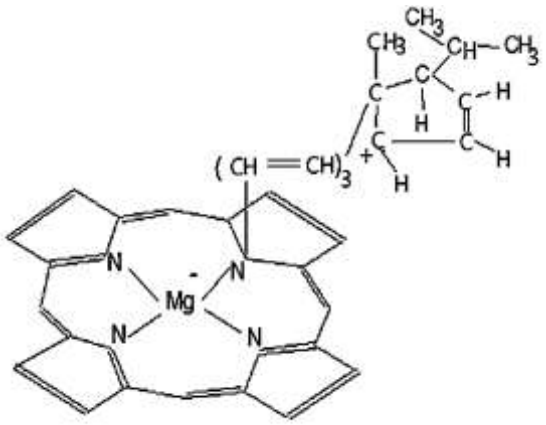
Fig. 7: Mg.1,6-(2-dehydro-5-isopropyl-1-methyl cyclopentan-3-en-1yl) hex-1,3,5-trien-1-yl.porphin (truncated)

Two further reactions are needed to close the C-ring with the truncated side-chain, as follows:

3.29 The Formation of Mg.1,porphin.6-(2-dehydro-5-isopropyl-1-methyl cyclopentan-3-en-1yl) hex-1,3,5-trien-N1-yl.

The promotion to the higher N-bound state of the adduct may be represented as,

Mg.1, 6-(2-dehydro-5-isopropyl-1-methyl cyclopentan-3-en-1yl) hex-1,3,5-trien-1-yl. porphin (49) →



Mg.1.porphin.6-(2-dehydro-5-isopropyl-1-methyl cyclopentan-3-en-1yl) hex-1,3,5-trien-1-yl
. (47)

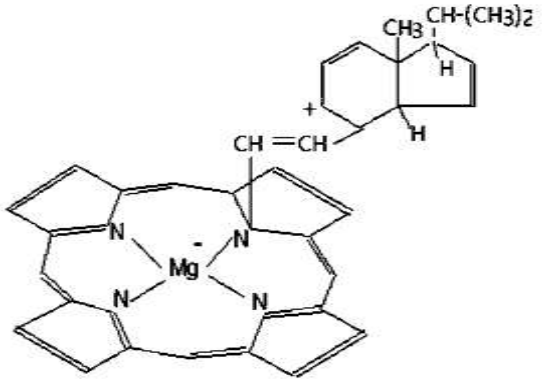
$$\Delta H = -0.43743 \text{ h}$$

The activation energy was the same as the enthalpy change. The charge on the adduct was -0.29.

3.30. The Formation of Mg.1,porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl

The cyclisation involving the rotations previously considered, [16], [40], is represented as,

Mg.1,porphin,6-(2-dehydro-5-isopropyl-1-methyl cyclopentan-3-en-1yl) hex-1,3,5-trien-1-yl →



Mg.1,porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl (48)

$$\Delta H = -0.12890 \text{ h}$$

The activation energy involves rotations, [16], [40], and the charge on the adduct was -0.34. The closure of this C-ring determines the trans C-D rings and the steroid β-methyl substituent at C-13.

This sequence produces the D and C rings of ergosterol, Fig. 8.

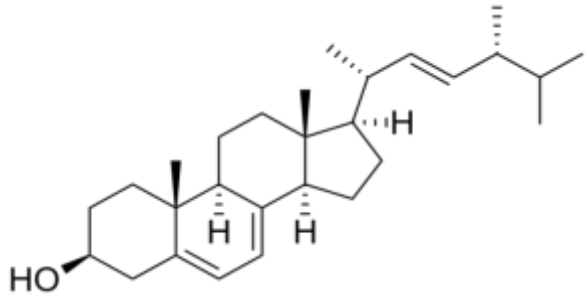
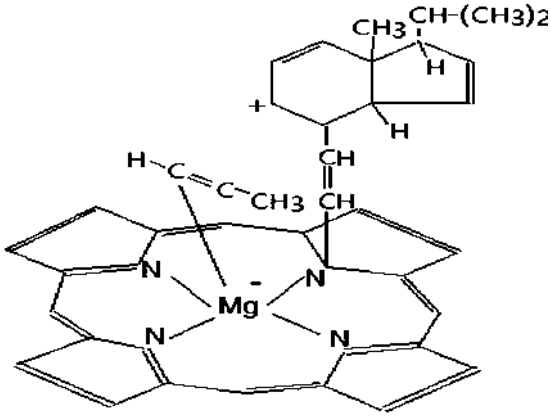


Fig. 8: ergosterol.

3.31 The Formation of Mg.1,propynyl. porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl

The Mg.1,porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl)-ethen-N1-yl may add a further propyne molecule on the vacant magnesium site as,

propyne + Mg.1,porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl. →



Mg.1,propynyl.porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl (49)

$$\Delta H = -0.15372 \text{ h}$$

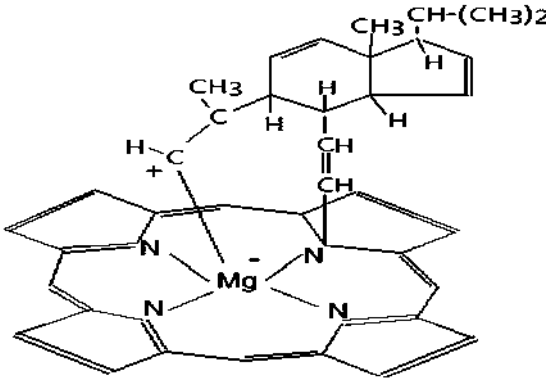
No activation energy was found for this charge transfer addition reaction.

The charge on the adducts was: propyne, 0.045, and the indenyl entity, 0.190.

3.32. The Formation of Mg.1,2-(9H-4-ethen-N2-yl-1-isopropyl-8-methyl inden-5-yl) propen-1-yl.porphin.

The Mg.1,propynyl.porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl may cyclise with the formation of the trans B-C bridge as,

Mg.1,propynyl.porphin.2-(9H-1-isopropyl-8-methyl-inden-4-yl) ethen-N1-yl →



Mg.1,2-(9H-4-ethen-N2-yl-1-isopropyl-8-methyl inden-5-yl) propen-1-yl.porphin (50)

$$\Delta H = \quad 0.00153 \quad h$$

The potential energy surface for the bonding is shown as,

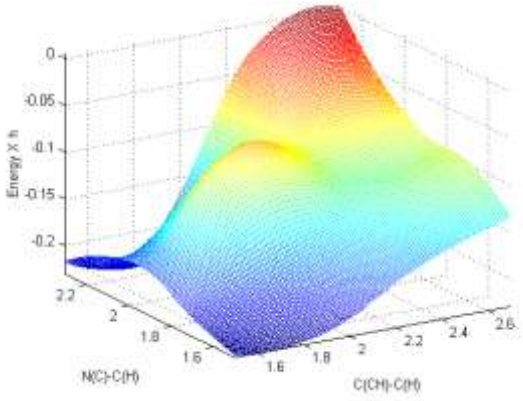


Fig. 9: The potential energy surface showing the contraction of the $C(CH_3)$-C(H) bond between the propyne adduct and the N-bound entity as the N-C(H) bond of the inden-4-yl bond to the porphin ring is enlarged. The reactant is at (2.6,1.6), the product at (1.6,1.6). The N-C dissociated product at (1.6,2.2). The energy is -1882 + X h.

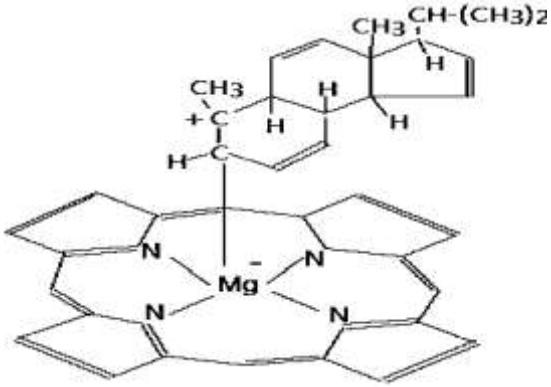
The graph (Fig. 9) does not show any discernable activation energy for the bonding.

The charge on the adduct was -0.186.

3.33 The Formation of Mg.1,des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.porphin

The Mg.1,2-(9H-4-ethen-N2-yl-1-isopropyl-8-methyl inden-5-yl) propen-1-yl.porphin
may cyclise as,

Mg.1,2-(9H-4-ethen-N2-yl-1-isopropyl-8-methyl inden-5-yl) propen-1-yl.porphin →



Mg.1,des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.porphin (51)

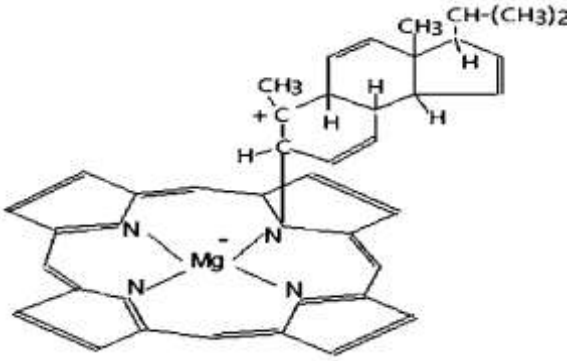
$$\Delta H = \quad -0.06217 \quad h$$

No activation energy could be recorded during the scan for this bonding. The charge on the adduct was 0.114

3.34 The Formation of Mg.1,porphin. des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.

The Mg.1,des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.porphin may be excited to a higher energy state as,

Mg.1,des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.porphin →



Mg.1,porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl. (52)

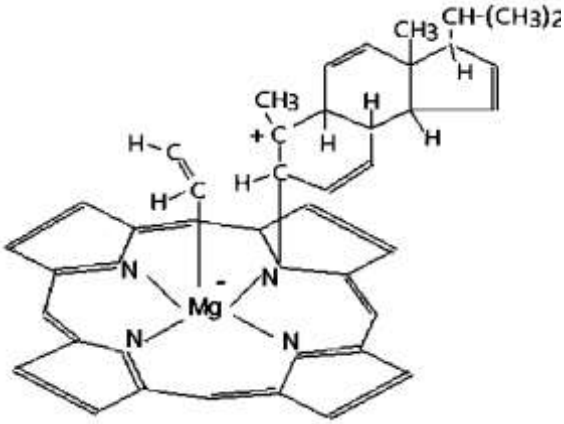
$$\Delta H = \quad 0.02609 \quad h$$

The activation energy was the same as the enthalpy change. The charge on the adduct was 0.34.

3.35 The Formation of Mg.1,ethynyl. porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-N5-yl.

The Mg.1,porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.
may add a further ethyne adduct as,

ethyne + Mg.1,porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-5-yl.
→



Mg.1,ethynyl. porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-N5-yl (53)

$\Delta H = -0.03189$ h

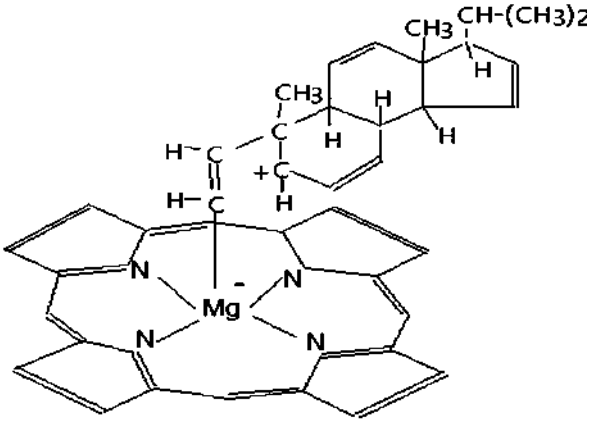
No activation energy was recorded for this bonding addition.

The charge on the ethyne adduct was 0.083, and that on the phenanthrenyl entity 0.575. These change at the transition state for the adducts to bond.

3.36 The Formation of Mg.1,2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl)-ethen-1-yl.porphin

The Mg.1,ethynyl.porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-N5-yl. may bond as,

Mg.1,ethynyl.porphin.des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-N5-yl.
→



Mg.1,2-(des-A-6,7,11,12,15,16-hexa-dehydro-pregnan-10-yl)-ethen-1-yl.porphin (54)

$\Delta H = -0.02728$ h

The form of the potential energy surface for the bonding is shown in Fig. 10.

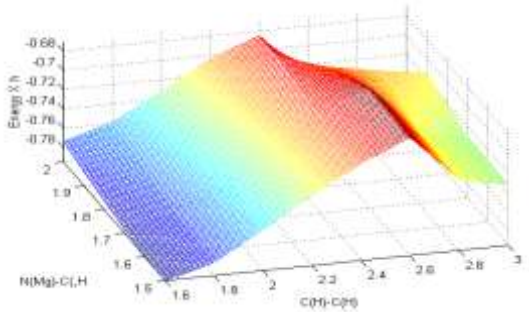


Fig. 10: The reactant is near (3.0,1.5), the product at (1.6,1.5). The saddle point is near (2.5,1.9). The N-C dissociated product at (1.5,2.0). The energy is -1954 + X h.

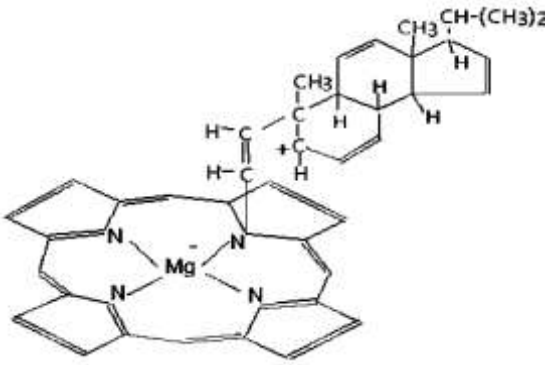
The activation energy for bonding was 0.03 h, that for scission, 0.11 h.

The charge on the adduct was 0.053.

3.37 The Formation of Mg.1,porphin.1,2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl)-ethen-N1-yl.

Excitation of the Mg.1,2-(des-A-6,7,11,12,15,16-hexa-dehydro-pregnan-10-yl)-ethen-1-yl.porphin may lead to severance of the Mg-C bond and promotion of the adduct to the higher energy state as,

Mg.1,2-(des-A-6,7,11,12,15,16-hexa-dehydro-pregnan-10-yl)-ethen-1-yl.porphin →



Mg.1,porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-N1-yl. (55)

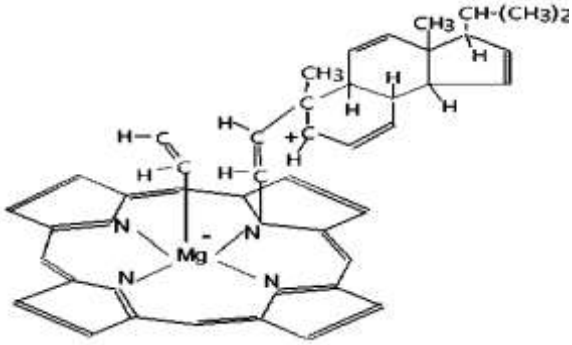
$$\Delta H = -0.02678 \text{ h}$$

The activation energy was the same as the enthalpy change. The charge on the adduct was 0.212.

3.38 The Formation Mg.1,ethynyl. porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl)-ethen-1-yl

The Mg.1,porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-1-yl may add a further ethyne molecule as,

ethyne + Mg.1,porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-1-yl . →



Mg.1,ethynyl.porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-N1-yl (56)

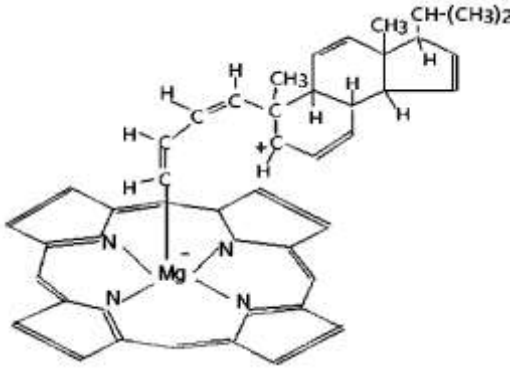
$$\Delta H = 0.07456 \text{ h}$$

The charge on the ethyne was 0.01, and that on the phenanthrenyl adduct 0.212.

3.39 The Formation of Mg.1,4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-1-yl.porphin

The Mg.1,ethynyl.porphin. 2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-N1-yl may bond as,

Mg.1,ethynyl.porphin.2-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) ethen-N1-yl →



Mg.1,4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-1-yl.porphin (57)

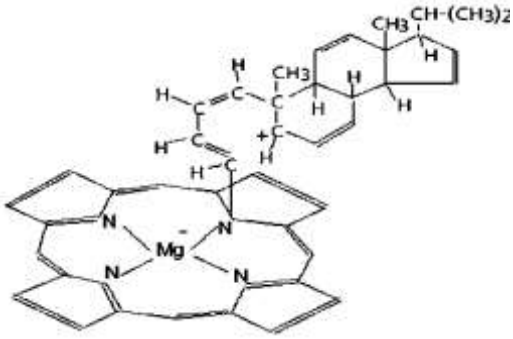
$$\Delta H = -0.13497 \text{ h}$$

The activation energy for bonding was 0.03 h , and for the reverse reaction 0.11 h. The charge on the adduct was 0.210.

3.40 The Formation of Mg.1,porphin.4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-N4-yl.porphin

The Mg.1,4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-1-yl.porphin may be promoted to the higher energy state as,

Mg.1,4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-1-yl.porphin →



Mg.1,porphin.4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-N4-yl. (58)

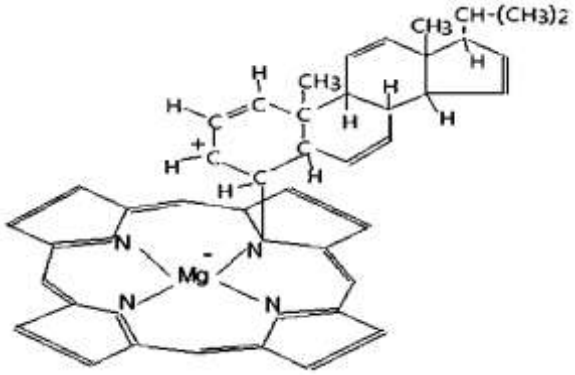
$\Delta H = -0.02089$ h

The charge on the adduct was 0.231.

3.41 The Formation of Mg.1,porphin. 3-dehydro 1,2,6,7,11,12,15,16-nonan-dehydro-pregnan-4-y.porphin.

The Mg.1,porphin.4-des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-N4-yl may bond as,

Mg.1,porphin.4-(des-A-6,7,11,12,15,16-hexa-dehydro-20-methyl pregnan-10-yl) but-1,3-dien-N4-yl. →



Mg.1,porphin 1,2,3,6,7,11,12,15,16-nonan-dehydro-20-methyl pregnan-4-yl (59)

$\Delta H = 0.01564$ h

No activation energy to close the ring was recorded The charge on the adduct was -0.321.

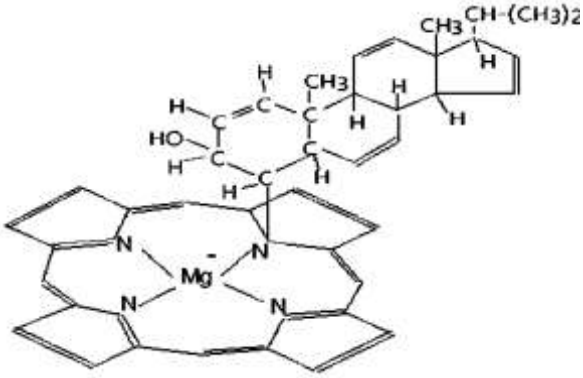
3.42 The Formation of Mg.1,porphin.3-hydroxy-20-methyl-1,2,6,7,11,12,15,16-octa-dehydro- pregnan-N4-yl).

The Mg.1,porphin 1,2,3,6,7,11,12,15,16-nonan-dehydro-20-methyl pregnan-4-yl. maybe susceptible to reaction with hydroxyl radicals or anions in the environment, [24], as,

$H_2O \rightarrow H^+ + OH^{-1}$ $\Delta H = 0.67114$ h

$H_2 \rightarrow 2H\cdot$ $\Delta H = 0.13826$ h

Mg.1,porphin 1,2,3,6,7,11,12,15,16-nonan-dehydro-20-methyl pregnan-4-yl.
$+ OH^-$ →



Mg.1,porphin.3-hydroxy-20-methyl 1,2,6,7,11,12,15,16-octa-dehydro-pregnan-N4-yl)$^-$ (60)

$\Delta H = -0.14300$ h

As the molecule is in the excited state then this reaction is more favourable. The charge on the adduct was 0.287.

3.42.1 The Formation of Mg.1,porphin. 1,2,6,7,11,12,15,16-octa-dehydro-1-hydroxy-20-methyl pregnan-4-yl).porphin

In the formation of the cholecalciferol A-ring substituents, there is an equally facile reaction at the C3-site with hydroxyl anion, or at the C1 and C3-sites with hydroxyl radical. This may occur whether the B-ring forms or not.

Mg.1,porphin 1,2,3,6,7,11,12,15,16-nonan-dehydro-20-methyl pregnan-4-yl + OH^{-1} →

Mg.1,porphin. 2,3,6,7,11,12,15,16-octa-dehydro-1-hydroxy-20-methyl pregnan-N4-yl)$^-$ (61)

$\Delta H_{(MP2)} = -0.07767$ h

Mg.1,porphin 1,2,3,6,7,11,12,15,16-nonan-dehydro-20-methyl pregnan-4-yl + 2 $OH\cdot$ →

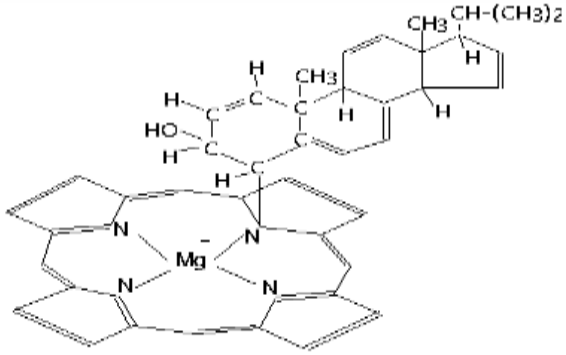
Mg.1,porphin. 2,6,7,11,12,15,16-heptan-dehydro-1,3-dihydroxy-20-methyl pregnan-N4-yl (62)

$\Delta H_{(MP2)} = -0.05233$ h

3.43. The Formation of Mg.1,porphin. 1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-4-yl).porphin$^-$

Mg.1,porphin.1,2,6,7,11,12,15,16-octa-dehydro-3-hydroxy-20-methyl pregnan-4-yl).porphin$^-$ may lose hydrogen by hydrogen free radical abstraction as,

Mg.1,porphin.1,2,6,7,11,12,15,16-octa-dehydro-3-hydroxy-20-methyl pregnan-4-yl).porphin$^-$ + 2H$^{\cdot}$ → $2H_2$ +



Mg.1,porphin.1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-N4-yl).porphin$^-$ (63)

$$\Delta H = -0.12282 \text{ h}$$

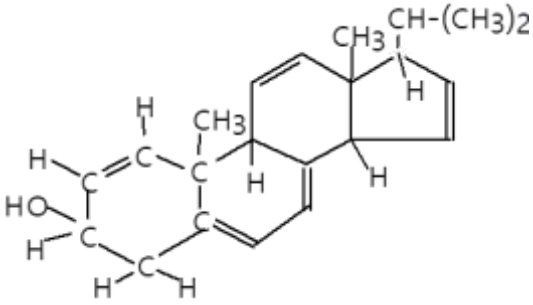
The charge on the adduct was 0.700.

This abstraction may alternately operate at the C8 and C9 to form the lanosterol group, [23].

3.44 The Formation of 1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnane

The Mg.1,porphin. 1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-N4-yl).porphin$^-$ may react with a proton to release the adduct from the catalyst as a neutral molecule as,

Mg.1,porphin.1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-4-yl).porphin$^-$ + H^+ → Mg.porphin +

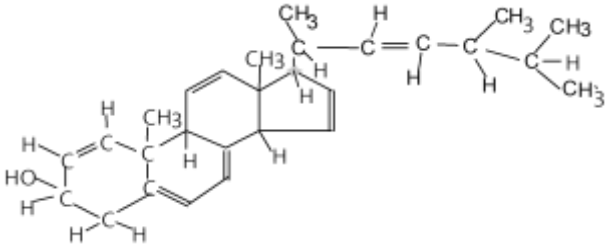


1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnane (64)

$$\Delta H = -0.62914 \text{ h}$$

3.45 The Formation of 1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-ergostane

At this point in the synthesis with the catalyst separated, the fully extended side-chain was restored for the molecule to be depicted as,



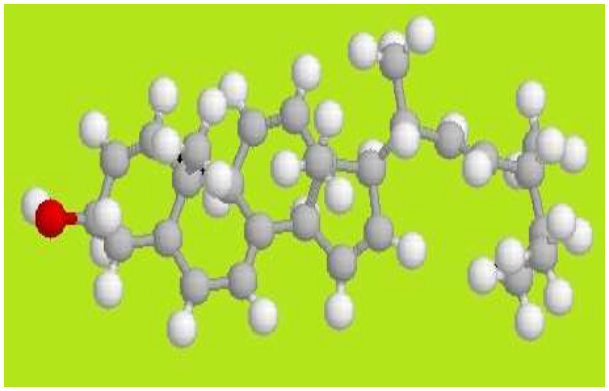
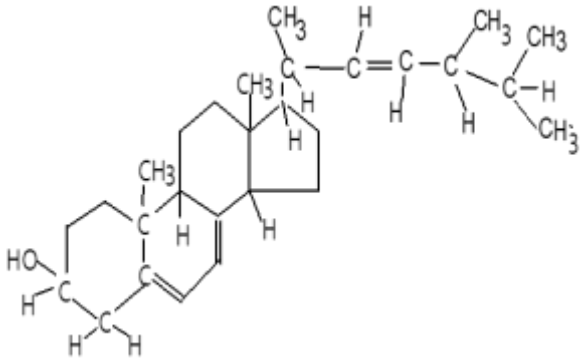


Fig. 11: 1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-ergostane

Further hydrogenation allows the natural substance to be designated as,

1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-ergostane + $3H_2$ →



3-hydroxy-ergostane (65)

$$\Delta H = -0.05264 \text{ h}$$

3.46 The Formation ergocalciferol (Vitamin D_2)

The ergosterol may under photolysis give Vitamin D_2, as in the synthetic reaction, [3]. The prebiotic synthesis may have proceeded similarly.

Although the B-ring closure is not necessary to form ergocalciferol, it is assumed here that the B-ring closed and it is necessary for the scission of the steroid C9-C10 bond to occur as shown in, Fig. 12, for the potential energy diagram of Mg.1,porphin. 1,2,5,6,7,8, 11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-N4-yl). The potential energy diagram indicates that the internal coordinates chosen as stretching of this bond accompanied by a rotation of the dihedral angle, C5-C6-C7-C8, in the presence of a hydroxyl anion near a C19 hydrogen atom. there is a feasible scission of the C9-C10 bond with an activation energy of 0.15 h, well within the range of the first excitation of the molecule, 0.24 h. It also indicates that considerably more activation energy is required to produce the trans, C5-C6-C7-C8, isomer. No abstraction of the methyl hydrogen atom occurs at a hydroxyl anion distance of 1.4 A, but at 1.0 A, abstraction occurs.

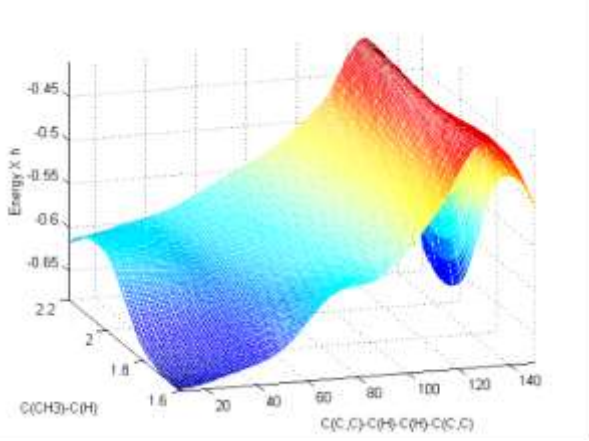


Fig. 12: The potential energy diagram for Mg.1,porphin.1,2,5,6,7,8, 11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-N4-yl). The y-axis shows the stretching of the C9-C10 bond, whilst the x-axis shows rotation around the dihedral angle, C5-C6-C7-C8. The energy is -2180 + X h.

The scission appears also as free radical-mediated with scission of the C9-C10 bond and contraction of the C19 hydrogen – C10 coordinate.

The following sequence of reactions appears feasible after the scission of the C9-C10 bond to release the catalyst from the ercalciol precursor (truncated and not fully hydrogenated), Fig. 13, as,

Mg.1,porphin.1,2,5,6,7,8,11,12,15,16-deca-dehydro-3-hydroxy-20-methyl pregnan-N4-yl).porphin- + $H^+ \rightarrow$ Mg.porphin +

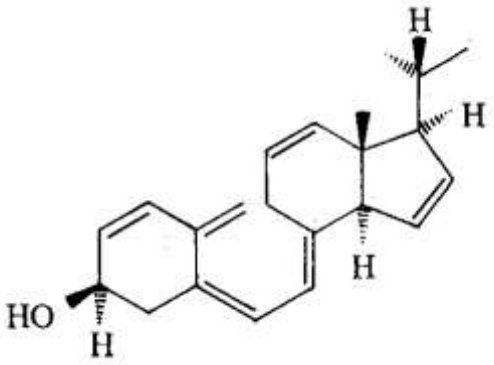


Fig. 13: 1,2,10,11,15,16-hexa-dehydro ercalciol

(66)

$$\Delta H = -0.59035 \text{ h}$$

It is assumed that the above formation of a dehydrogenated ercalciol, [2], is equivalent to the formation of ergocalciferol

3.47 The Formation of cholecalciferol (Vitamin D_3)

The reactant for the formation of cholecalciferol is 7-dehydrocholesterol, which differs from ergosterol in the D-ring side chain being fully hydrogenated and having one less methyl group replaced by a hydrogen atom. For the truncated molecules considered here, the reaction should be similar.

The present-day metabolic products of cholecalciferol, [3], 25-hydroxycholecalciferol and 1,25-dihydroxycholecalciferol should have all been freely available at the time of the prebiotic synthesis of ergocalciferol and cholecalciferol.

4 Conclusion

Steroids have been regarded as composed of isoprene units, [3], but catalysis suggests that at an earlier prebiotic time, the isoprene units themselves may have been formed by the copolymerization of the interstellar gases ethyne and propyne, inevitably, according to the laws of chemistry. These are also both readily available from the reaction of carbides and allylides in aqueous solution, [25]. The catalyst used here, Mg.porphin, essential to present biochemistry, should have enabled the synthesis of ergosterol at the time of photosynthesis, [26], at some 3.4 billion years, and vitamin D is recorded in phytoplankton in the ocean as photosynthesizing vitamin D for more than 500 million years, [27], [28]. The catalyst, here taken as Mg.porphin formed from the same atmosphere, [12], enables individual steps in the sequence to be activated to a limit of about 0.21 h, dependent on the radiation

level present in prebiotic times and the temperature. It is a surface, photochemically activated catalyst for a wide range of substrates that only weakly interact with it as charge transfer or van der Waal complexes, [21], [22]. It can severely limit the configurations that are preferentially available to a growing polymer as here. It provides a plausible explanation for the three trans bridges: C:D/B:C/A: B, the steroid C10, C13, and C17 β-substituents, the 3-hydroxyl substituent, the dehydrogenation and the stereochemistry, where steric effects and charges in the presence of the exciting magnetic field may have been determinant.

The very many configurations possible from the three fused rings allow 2^3 gross morphological structures, but these need not be strong contenders for the vitamin D receptors (VDRs) presently studied, [29]. Also, the energy change between axial and equatorial substituents appears minimal, [30]. The production of derivatives that may select specific enhanced outcomes is considerable, [31], and several have been approved. It is some justification for the proposed sequence that the derivatives involving the 1 and 25 hydroxyl groups together with the scission of the A-B ring system by ultraviolet light (UVB), [32], are predicted and accessible, as is the most stable form of the ergosterol in the predominantly chair or quasi-chair conformation, [33].

The formation of the prebiotic steroids essential to the biochemistry of plants, [34], and mammals, [35], but not insects, [36], preceded their incorporation into molecular evolution and biochemistry some 350 million years ago, at least, [37], and their stability and importance over such a time period are apparent.

Until the bonding energies of the VDRs are calculated the alteration and manipulation of the sequence will be less informed. Mutations, [4], [38] also affect this on an experimental basis and are a fruitful field of research. Ab initio studies greatly augment experimental research and provide a satisfactory understanding of the prebiotic world.

Further work at a higher accuracy may alter the values given here.

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