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Diels-Alder Reactions of Ni(II) β-Vinyl-*meso*-Tetraarylporphyrins

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***Abstract*:** The cycloaddition reactions of nickel(II) β-vinyl-*meso*-tetraphenylporphyrins with tetracyanoethylene (TCNE) in chloroform, afford [2+2] adducts containing a cyclobutane ring and [4+2] adducts. The [2+2] adducts can also be produced by rearrangement of the [4+2] chlorins.

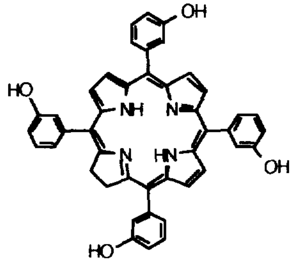
Certain chlorin and other porphyrin derivatives are being evaluated as second generation photosensitizers in the photodynamic therapy (PDT) of neoplastic lesions.[1] Some of the former compounds have been obtained from chlorophyll a and others, such as (**1**), by reduction of the corresponding porphyrins. Similar macrocycles have been also obtained by Diels-Alder reactions of β-vinylporphyrins with dienophiles.

It has been reported that protoporphyrin-IX dimethyl ester (**2**) reacts with a variety of dienophiles involving the vinyl groups and the neighbouring peripheral double bonds. The products obtained are isomeric mono- and bis-adducts of porphyrins, chlorins or isobacteriochlorins.[2] It was observed that no reaction took place on the iron(III) or nickel(II) complexes of protoporphyrin-IX dimethyl ester. In some cases[3,4] [2+2] and [4+2] cycloadditions took place and a variety of products, mainly chlorins, were obtained. In this way Diels-Alder processes have become very important in the synthesis of new tetrapyrrolic photosensitizers. To our knowledge β-vinyl-*meso*-tetraphenylporphyrin derivatives have not yet been used in such studies. However chlorin (**1**), derived from the correspondent porphyrin, behaves as a prominent compound in PDT studies.[1] Therefore our strategy was to synthesize β-vinyl-*meso*-tetraphenylporphyrin derivatives and to study their Diels-Alder cycloadditions with several dienophiles.

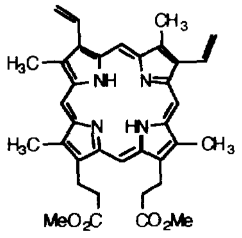
We now report the first results from cycloaddition reactions of the nickel complexes (**4**) of monovinyl-tetraarylporphyrin with TCNE, in chloroform at 0ºC and at room temperature. The vinyl group was readily introduced via the Vilsmeier formylation of (**3**) using $POCl_3$/DMF, followed by the Wittig reaction using CH_3PPh_3Br/NaH/THF.[5] Porphyrins (**4a,b**) readily reacted with an excess of TCNE to produce a mixture of products, the major ones being the [4+2], (**5**), and [2+2] adducts (**6**). The reaction was followed by 300 MHz ^1H- and ^1H-^1H COSY NMR spectroscopy at 0ºC. Products (**5**) and (**6**) were also identified by MS [FAB+; *m/z*=825 for the parent ion of (**5a,6a**) and *m/z*=945 for (**5b,6b**)], by UV/Vis spectrometry, since products (**6a,b**) are porphyrins (λ_{max}=570 nm) and (**5a,b**) are chlorins (λ_{max}=625 nm) and, in the case of (**6a**), by elemental analysis.[6] By NMR we observed that chlorins (**5**) rearranged to give porphyrins (**6**). After 5 hours at room temperature, or overnight at 0ºC, the [2+2] adduct (**6**) was the only product present [for (**6a**): δ_{H_2}=9.18 ppm (s), δ_{H_a}=4.61 ppm (dd, J=8.5 and 11.9 Hz), δ_{H_b}=3.52 ppm (t, J=12.1 Hz) and δ_{H_c}=3.10 ppm (dd, J=8.5 and 12.1 Hz); for (**6b**): δ_{H_2}=9.21 ppm (s), δ_{H_a}=4.73 ppm (dd, J=8.6 and 11.8 Hz), δ_{H_b}=3.62 ppm (t, J=12.1

Hz) and δH_c=3.22 ppm (dd, J=8.5 and 12.2 Hz)]. NOE experiments showed the proximity of the β-proton H_2 to H_b and the non-proximity of H_2 to H_a. From these results it can be concluded that there is no free rotation of the cyclobutane ring and that the [2+2] adduct is the thermodynamically stable product.

Work is in progress in our laboratory to study the behaviour of other β-vinyl-*meso*-tetraarylporphyrin derivatives with other dienophiles.



1



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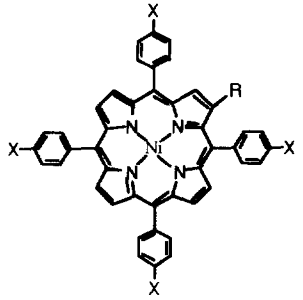
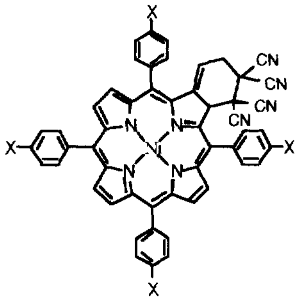


3 : R=H
4 : R=CHCH$_2$

a : X=H
b : X=OCH$_3$



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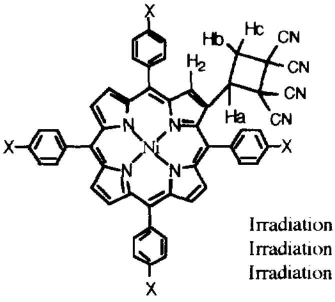

6

Irradiation of H_2-->NOE on H_b (6%)
Irradiation of H_b-->NOE on H_2 (13%) and H_c (21%)
Irradiation of H_a-->NOE on H_c (7%)

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6. Anal. Calcd. for $C_{52}H_{30}N_8Ni$: C, 75.65; H, 3.66; N, 13.57%. Found: C, 75.23; H, 3.79; N, 13.41%.

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