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Novel porphyrin-quinone architectures via 1,3-dipolar cycloaddition reactions

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Abstract—Porphyrinic pyridinium ylides react with 1,4-benzoquinone and 1,4-naphthoquinone to afford novel *meso*-substituted indolizine porphyrins.

Nature has built up complicated photosystems over billions of years for photochemical conversion and storage of energy. During the last decades, a great number of biomimetic model systems have been used to study the photosynthetic electron-transfer mechanism.[1] Therefore, numerous covalently linked porphyrin-quinone compounds, with different bridging features, have been designed and studied for that purpose.[2]

Over the past years, we[3,4] and others[5] have been investigating the reactivity of porphyrins as dienophiles and dipolarophiles in Diels–Alder and 1,3-dipolar cycloaddition reactions.[6] As part of such studies, we have used new porphyrin pyridinium salts as precursors of the corresponding ylides and investigated their reactivities with quinones. It is known from the literature that in 1,3-dipolar cycloadditions involving pyridinium salts, the dipolarophiles are usually dialkyl acetylenedicarboxylates or α-bromo-α,β-unsaturated esters or nitriles;[7] when electron-deficient alkenes are used as dipolarophiles the indolizine products are only isolated if the reactions are carried out in the presence of an oxidant (e.g., tetrakispyridinecobalt(II) dichromate or MnO_2).[8] In our present studies, the quinones were used in excess, acting as reagents and as oxidants.

We started these studies with the reaction of porphyrin-pyridinium salt **1**[9] with 1,4-benzoquinone in the presence of a base (K_2CO_3 or DBU).[10] As indicated in Scheme 1, the 1,3-dipolar cycloaddition product formed in this reaction depends on the base used. When potassium carbonate was used, only the mono-addition compound **2** (16% yield) was obtained; however, with DBU, bis-addition occurred and the novel porphyrinic dimer **3** (23% yield) was the only isolated addition product. In both cases, porphyrin **4** was also formed.

The structures of compounds **2** and **3** were deduced from their ^{1}H and ^{13}C NMR spectra, UV–vis and mass spectra.[11,12] The ^{1}H NMR spectrum of **2** shows a singlet at δ 4.18 ppm, corresponding to the methyl ester group, and an AB spin system at δ 6.81 and 6.83 ppm (J = 10.3 Hz), corresponding to the two proton resonances of the quinone moiety. The three protons at the indolizine ring appear as three double doublets at δ 8.05 (J = 1.9 and 7.3 Hz), 9.29 (J = 0.9 and 1.9 Hz) and 9.71 ppm (J = 0.9 and 7.3 Hz), while the protons of the *meso*-phenyl groups appear as two multiplets at δ 7.74–7.80 and δ 8.21–8.24 ppm. The eight β-pyrrolic protons appear as two AB spin systems at δ 8.86 (4H, J = 4.8 Hz) and 8.90 ppm (4H, J = 4.8 Hz). The ^{13}C NMR spectrum of compound **2** shows the signals corresponding to the three carbonyl groups at δ 161.8 ppm (ester group) and at δ 181.3 and 182.1 ppm (quinone). The FAB mass spectrum shows peaks at *m/z* 794 and 793, which are two units higher than the expected. Presumably, this might be due to the reduction of the quinone moiety, under the FAB conditions, and the observed peaks correspond to $[M+3H]^+$ (794) and to $[M+2H]^{+\cdot}$ (793).[13]

Keywords: Porphyrins; Ylides; Cycloadditions; Quinones; Indolizine.
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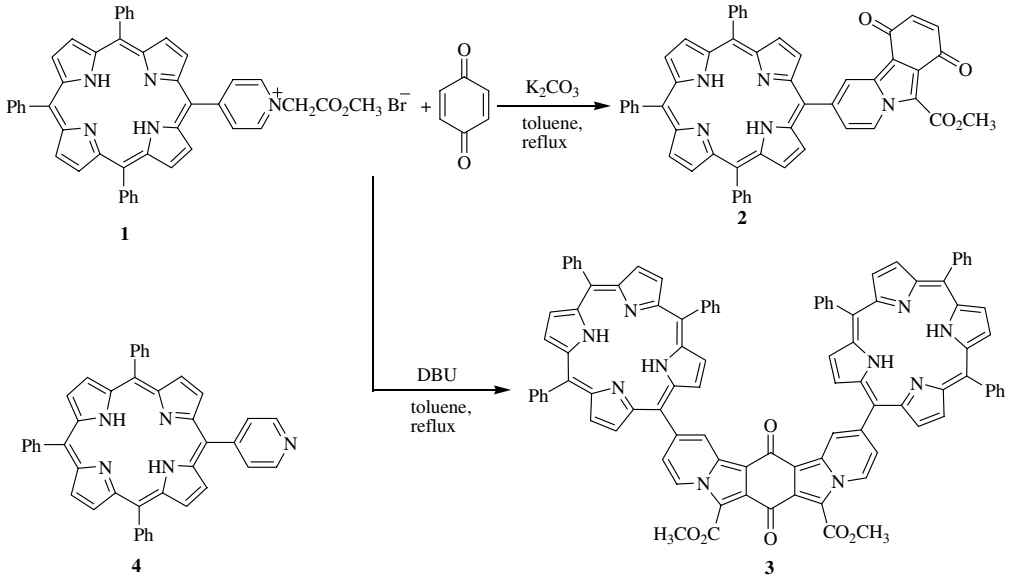
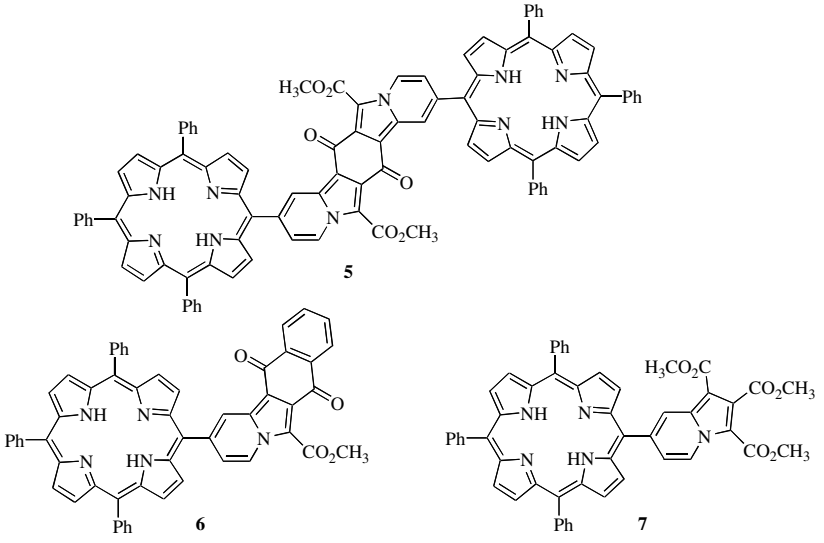


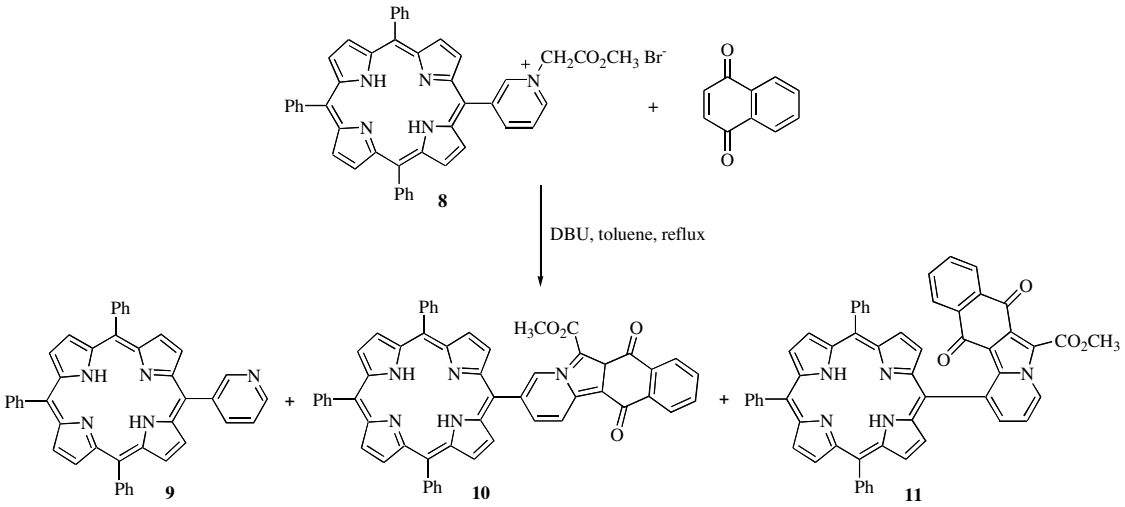
Scheme 1.

When we compare the ^{1}H NMR spectrum of **3** with the one of compound **2**, the main difference is the absence of the signals corresponding to the protons of the quinone moiety. This is clear evidence that a bis-addition occurred. The mass spectrum of this compound shows intense peaks at *m/z* 1475 ($[M+H]^{+}$) and 1474 ($[M]^{+\cdot}$), confirming that it is in fact a bis-addition product. The addition of a second porphyrinic pyridinium ylide to compound **2**, followed by aromatisation, could lead to compound **3** or to its isomer **5**. However, only one of them was formed. The ^{13}C NMR spectrum of the compound shows three signals corresponding to carbonyl groups: one at δ 162.2 ppm corresponding to the ester group, and the other two at δ 177.5 and 177.9 ppm corresponding to the carbonyl groups of the quinone moiety. This spectrum only fits with structure **3**, since in structure **5** there are only two non-equivalent carbonyl groups. The formation of a mono-addition product when potassium carbonate is used while a bis-addition compound is formed in the presence of DBU is probably related to the fact that in the first case there is a two-phase reaction system, while with DBU it is a homogenous reaction.

Porphyrin **4**, a by-product of these reactions, results from the dealkylation of **1**. To confirm it, a toluene solution of compound **1** in the presence of DBU or K_2CO_3 (in the absence of any dipolarophile) was refluxed for 8 h and in fact it was converted into **4** (60% yield). It has been shown in the literature that the carbon–nitrogen bond cleavage in pyridinium compounds corresponds to the oxidation of the carbanion by oxygen.[14]

The cycloaddition reaction of pyridinium salt **1** with 1,4-naphthoquinone and with dimethyl acetylenedicarboxylate afforded, respectively, compounds **6** (16% yield)[15] and **7** (39% yield).[16]





Scheme 2.

The reaction of the pyridinium salt **8** with 1,4-naphthoquinone afforded the non-alkylated pyridyl porphyrin **9** (28% yield) and the two regioisomeric compounds **10** (10% yield)[17] and **11** (5% yield) (Scheme 2).[18] We are extending our studies to other dipolarophiles and to di- and tetrapyridyl substituted porphyrins. Collaborative theoretical studies related with the formation of type **3** compounds have also been initiated.

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9. Pyridinium salts **1** and **7** were obtained from the reaction of the corresponding porphyrins **4** and **8** with methyl bromoacetate in refluxing chloroform, a modification of the procedure described in Zhang, L.; Liang, F.; Sun, L.; Hu, Y.; Hu, H. *Synthesis* **2000**, 1733–1737.
10. Typical procedure: To a toluene (6 mL) solution of **1** (20 mg) and 1,4-benzoquinone (56 mg, 20 equiv) was added K_2CO_3 (180 mg, 50 equiv) [or DBU (0.19 mL, 50 equiv)]. The mixture was refluxed for 8 h. The reaction mixture was cooled to room temperature and the toluene was partially evaporated. The compounds were separated by column chromatography using chloroform as eluent and further purified by preparative TLC.
11. Selected data for compound **2**: mp >300 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −2.75 (s, 2H, NH), 4.18 (s, 3H, CO_2CH_3), 6.81 and 6.83 (AB, 2H, quinone CH, J = 10.3 Hz), 7.74–7.80 (m, 9H, Ph-H$_{meta,para}$), 8.05 (dd, 1H, Indolizine-H, J = 1.9 and 7.3 Hz), 8.21–8.24 (m, 6H, Ph-H$_{ortho}$), 8.86 (AB, 4H, β-H, J = 4.8 Hz), 8.90 (AB, 4H, β-H, J = 4.8 Hz), 9.29 (dd, 1H, Indolizine-H, J = 0.9 and 1.9 Hz), 9.71 (dd, 1H, Indolizine-H, J = 0.9 and 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 52.6 (CO_2CH_3), 111.7, 114.2, 115.3, 120.8, 121.2, 124.0, 125.1, 125.3, 126.8, 126.9, 127.9, 131.4, 131.8, 134.5, 134.6, 135.0, 139.2, 141.89, 141.91, 143.1, 146.4, 161.8 (CO_2CH_3), 181.3 and 182.1 (quinone CO). UV–vis ($CHCl_3$) λ_{max} (log ε): 420 (5.43), 516 (4.23), 556 (3.95), 590 (3.78), 649 (3.61) nm. MS (FAB) *m/z* 794 $(M+3H)^+$, 793 $(M+2H)^{+\bullet}$. Anal. Calcd for $C_{52}H_{33}N_5O_4$: C, 78.87; H, 4.20; N, 8.84. Found: C, 78.91; H, 4.23; N, 8.75.

12. Selected data for compound **3**: mp >300 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −2.86 (s, 4H, NH), 4.27 (s, 6H, CO_2CH_3), 7.64–7.73 (m, 18H, Ph-$H_{meta,para}$), 7.99 (dd, 2H, Indolizine-H, J = 1.9 Hz and J = 7.3 Hz), 8.07–8.15 (m, 12H, Ph-H_{ortho}), 8.77 (AB, 8H, β-H, J = 5.2 Hz), 8.81 (d, 4H, β-H, J = 4.9 Hz), 8.93 (d, 4H, β-H, J = 4.9 Hz), 9.38 (dd, 2H, Indolizine-H, J = 0.8 and 1.9 Hz), 9.61 (dd, 2H, Indolizine-H, J = 0.8 and 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 52.7 (CO_2CH_3), 114.6, 114.7, 115.8, 117.7, 120.5, 120.9, 122.4, 123.8, 125.0, 125.9, 126.6, 127.4, 127.7, 130.2, 131.1, 131.2, 131.3, 131.4, 131.6, 134.5, 134.7, 137.5, 141.7, 141.87, 141.90, 162.2 (CO_2CH_3), 177.5 and 177.9 (quinone CO). UV–vis ($CHCl_3$) λ_{max} (log ε): 419 (5.80), 517 (4.67), 557 (4.45), 590 (4.18), 649 (4.06) nm. MS (FAB) *m/z* 1475 $(M+H)^+$, 1474 $M^{+\cdot}$. Anal. Calcd for $C_{98}H_{62}N_{10}O_6$: C, 79.77; H, 4.24; N, 9.49. Found: C, 79.86; H, 4.15; N, 9.32.
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15. Selected data for compound **6**: mp >300 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −2.75 (s, 2H, NH), 4.24 (s, 3H, CO_2CH_3), 7.72–7.80 (m, 11H, naphth.-H and Ph-$H_{meta,para}$), 8.10 (dd, 1H, Indolizine-H, J = 1.9 and 7.3 Hz), 8.21–8.24 (m, 7H, naphth.-H and Ph-H_{ortho}), 8.31–8.34 (m, 1H, naphth.-H), 8.87 (AB, 4H, β-H, J = 4.8 Hz), 8.91 (d, 2H, β-H, J = 4.9 Hz), 8.95 (d, 2H, β-H, J = 4.9 Hz), 9.52 (dd, 1H, Indolizine-H, J = 0.9 and 1.9 Hz), 9.70 (dd, 1H, Indolizine-H, J = 0.9 and 7.3 Hz). UV–vis ($CHCl_3$) λ_{max} (log ε): 421 (5.54), 517 (4.33), 556 (4.10), 591 (3.84), 648 (3.73) nm. MS (FAB) 842 $(M+H)^+$, 841 $M^{+\cdot}$. Anal. Calcd for $C_{56}H_{35}N_5O_4$: C, 79.89; H, 4.19; N, 8.32. Found: C, 79.89; H, 4.25; N, 8.32.
16. Selected data for compound **7**: mp 273–274 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −2.76 (s, 2H, NH), 3.80, 4.05 and 4.11 (3s, 9H, $3 \times CO_2CH_3$), 7.73–7.79 (m, 9H, Ph-$H_{meta,para}$), 8.00 (dd, 1H, Indolizine-H, J = 1.9 and 7.2 Hz), 8.21–8.24 (m, 6H, Ph-H_{ortho}), 8.86–8.92 (m, 8H, β-H), 9.14 (dd, 1H, Indolizine-H, J = 0.9 and 1.9 Hz), 9.87 (dd, 1H, Indolizine-H, J = 0.9 and 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 51.7 (CO_2CH_3), 52.2 (CO_2CH_3), 53.1 (CO_2CH_3), 103.8, 112.1, 116.0, 120.7, 121.1, 122.4, 124.8, 125.2, 126.71, 126.74, 127.8, 131.6, 134.5, 136.7, 141.3, 141.88, 141.93, 160.7 (CO_2CH_3), 163.4 (CO_2CH_3), 166.3 (CO_2CH_3). UV–vis ($CHCl_3$) λ_{max} (log ε) 417 (5.32), 516 (4.30), 553 (3.99), 590 (3.78), 646 (3.63) nm. HRMS (ESI) Calcd for $C_{52}H_{38}N_5O_6$ $(M+H)^+$: 828.2786. Found 828.2817.
17. Selected data for compound **10**: mp >300 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −2.77 (s, 2H, NH), 4.01 (s, 3H, CO_2CH_3), 7.73–7.82 (m, 11H, naphth.-H and Ph-$H_{meta,para}$), 8.21–8.24 (m, 6H, Ph-H_{ortho}), 8.32–8.39 (m, 2H, naphth.-H), 8.41 (dd, 1H, Indolizine-H, J = 1.5 and 9.1 Hz), 8.87–8.94 (m, 8H, β-H), 9.01 (dd, 1H, Indolizine-H, J = 0.9 and 9.1 Hz), 10.13 (br s, 1H, Indolizine-H). UV–vis ($CHCl_3$) λ_{max} 420, 515, 551, 590, 645 nm. MS (FAB) 842 $(M+H)^+$, 841 $M^{+\cdot}$. HRMS (FAB) calcd. for $C_{56}H_{36}N_5O_4$ $(M+H)^+$: 842.2767. Found 842.2757.
18. Selected data for compound **11**: mp >300 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: −2.52 (s, 2H, NH), 4.25 (s, 3H, CO_2CH_3), 6.58 (dd, 1H, naphth.-H, J = 1.0 and 7.9 Hz), 7.01 (dt, 1H, naphth.-H, J = 1.2 and 7.6 Hz), 7.35 (t, 1H, naphth.-H, J = 7.1 Hz), 7.48 (t, 1H, Indolizine-H, J = 7.1 Hz), 7.70–7.78 (m, 9H, Ph-$H_{meta,para}$), 7.99–8.03 (m, 2H, Indolizine-H and naphth.-H), 8.15–8.25 (m, 6H, Ph-H_{ortho}), 8.64 (d, 2H, β-H, J = 4.8 Hz), 8.76 (d, 2H, β-H, J = 4.8 Hz), 8.84 (AB, 4H, J = 5.2 Hz), 9.56 (dd, 1H, Indolizine-H, J = 0.6 and 7.0 Hz). UV–vis ($CHCl_3$) λ_{max} 421, 517, 553, 593, 649 nm. MS (FAB) 842 $(M+H)^+$, 841 $M^{+\cdot}$. HRMS (FAB) Calcd for $C_{56}H_{36}N_5O_4$ $(M+H)^+$: 842.2767. Found 842.2780.