Pergamon

Bioorganic & Medicinal Chemistry Letters, Vol. 7, No. 20, pp. 2589-2592, 1997

0960-894X/97 $17.00 + 0.00

PII: S0960-894X(97)10027-0

NOVEL OXIDATION REACTIONS OF STERICALLY DEMANDING 3,6-DI-*TERT*-BUTYL PORPHYRIN-*O*-QUINONES TO MUCONIC ANHYDRIDE DERIVATIVES

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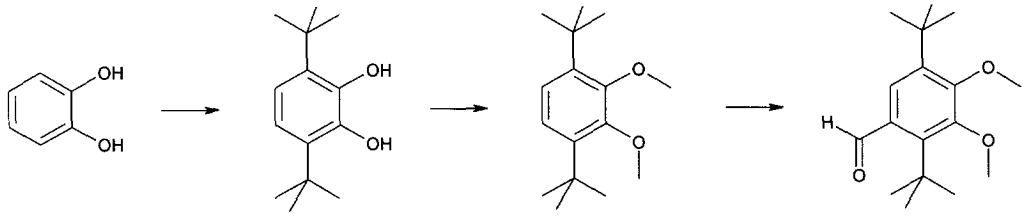
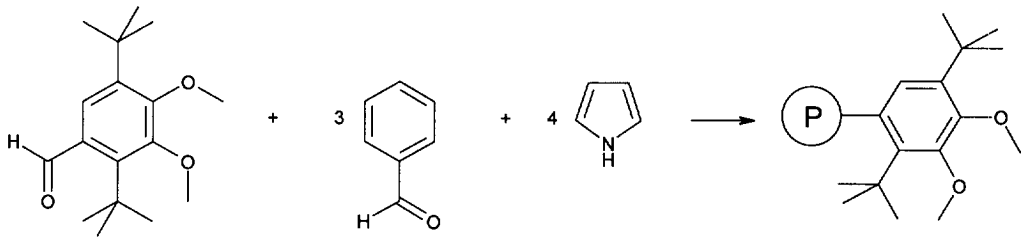
Abstract: Porphyrin quinones with sterically demanding 3,6-di-*tert*-butyl-*o*-quinones were synthesized for electron transfer studies. In the presence of atmospheric oxygen the covalently free base porphyrin-*o*-quinones are oxidized to muconic acid anhydride and 3,6-dicarbonyl-derivatives. In contrast to the well established chemistry of catecholase models based on 3,5-substituted quinones this is the first example for oxidative ring expansion of 3,6-disubstituted *o*-quinones. © 1997 Elsevier Science Ltd.

We have embarked on a comprehensive study of the electron-transfer properties of covalently-linked porphyrin quinones as models for the primary steps in photosynthesis.[1] In this context we became interested in the synthesis of stabilized porphyrin-*o*-quinones, which have not been described in the literature to date. As target compounds we chose a donor–acceptor compound with covalent linkage of a *meso*-triphenylporphyrin moiety to a symmetrical *o*-quinone (e.g., 3,6-di-*t*-butyl-*o*-quinone). *tert*-Butylated *o*-quinones are also of interest as model compounds for catecholase reactions. However, due to the difficult synthesis of symmetrically substituted *o*-quinones, the asymmetric 3,5-di-*t*-butyl-*o*-quinone (or the corresponding pyrocatechol) have been exclusively employed in studies on catecholase reactions.[2]

The synthesis of the porphyrin *o*-quinones started with preparation of the appropriate aldehyde **4**. Reaction of pyrocatechol with isobutylene in an autoclave after a modified Ershov procedure[3] gave the *t*-butylated pyrocatechol **2** in 75 % yield; small amounts of tri-*t*-butylated side products were detected spectroscopically. Pyrocatechol **2** was converted into the dimethyl ether **3**[4] followed by a formylation with $TiCl_4$ catalysis to **4** in 57% yield according to the method given by Rieche.[5] Intermediary preparation of **3** is necessary to prevent reaction of **2** to catecholates during formylation.



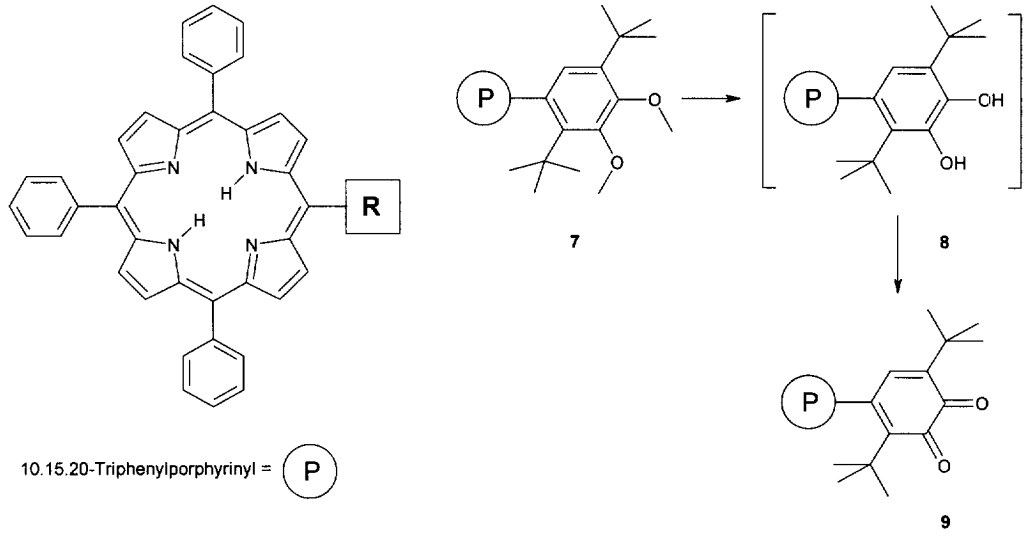
1 **2** **3** **4**



4 5 6 7

Final step in the synthesis of the desired porphyrin–quinone precursor **7** was reaction of aldehyde **4** with benzaldehyde **5** and pyrrole **6**. Boron trifluoride etherate and ethanol were employed as catalysts and the condensation was performed at a concentration of 10^{-2} M in a modification of the "Lindsey conditions"[6] to account for the sterically demanding aldehyde **4**.[7] Porphyrin **7** was obtained in 4% yield.

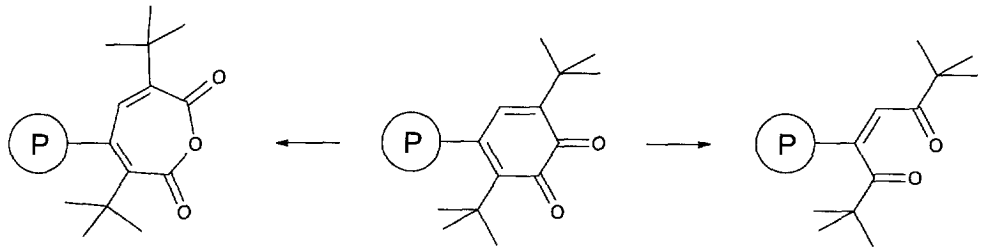
The substituted pyrocatechol dimethyl ether derivative **7** was demethylated using a 20-fold excess of boron tribromide. TLC showed that the demethylated product **8** was immediately oxidized by atmospheric oxygen to the target compound **9**. After workup (extraction with $NaHCO_3$ solution and water followed by drying with anhydrous Na_2SO_4) and chromatographic purification (silica gel, eluent dichloromethane/*n*-hexan = 1/1, v/v) , a crude product fraction was obtained.



10.15.20-Triphenylporphyrinyl = P

7 8 9

The 500 MHz ^{1}H NMR spectra of the product fraction indicated two different porphyrins that were formed in a ratio of 1:3.7, which were identified as the desired product **9** and the novel 1,4-dicarbonyl derivative **11**. During attempts to purify porphyrin **9** formation of a third porphyrin was observed. Single crystal X-ray crystallography (Fig. 1) showed this product to be the muconic acid anhydride **10**.[8]



10 **9** **11**

Under standard reaction conditions (air, daylight) no further oxidation of the porphyrins was observed. Additional investigations showed that the quinone **9** rapidly undergoes a complete oxidation to the described products under irradiation (3 min, 300 W lamp). In the absence of light a solution of the purified porphyrin-*o*-quinone **9** showed only partial formation of the oxidation products after 12 h. Irradiation of a 1:5 mixture of tetraphenylporphyrin and 3,6-di-*t*-butyl-1,2-benzoquinone under similar conditions in oxygenated $CDCl_3$ yielded no oxidation products. Additionally, neither the zinc complex of **9** nor the corresponding 3,6-dimethyl-4-(10,15,20-triphenylporphyrin-5-yl)-1,2-benzoquinone underwent these oxidative reactions. Thus, the oxidation is coupled to the covalent linkage and the presence of both a photochemically active free base porphyrin and 3,6-di-*t*-butyl-1,2-benzoquinone. Formation of related muconic acid derivatives has so far been described only for 3,5-di-*t*-substituted-*o*-quinones[9] while the 1,4-diketone derivatives of *o*-quinones present a novel class of oxidation products.

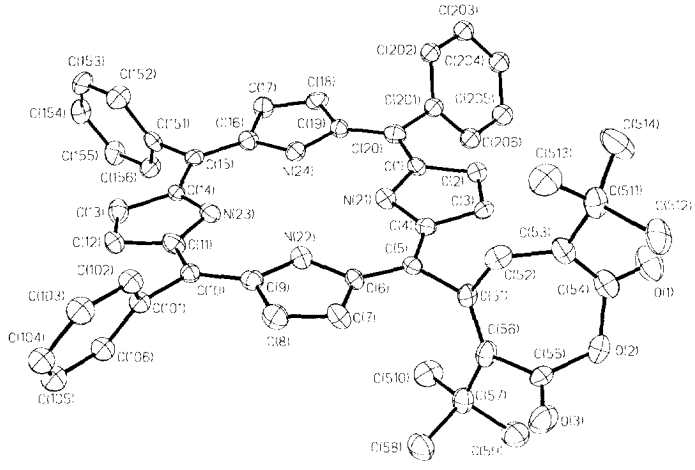


Figure 1. The molecular structure of **10** in the crystal. Hydrogen atoms have been omitted for clarity. Ellipsoids show 50 % occupancy.

Compounds **10** and **11** are porphyrins with high synthetic potential for further derivatizations. Both oxidation products **10** and **11** must be formed via competing reaction pathways since formation of the diketone **10** via the muconic acid anhydride **11** is not possible for stoichiometric reasons. Thus, we are currently investigating the electron transfer properties of **9**, the reaction mechanism for formation of the oxidation products, and the synthetic utility of the novel porphyrins.[10]

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft (SFB 337, Se543/2-4/3-1) and the Fonds der Chemischen Industrie. We are indebted to Professor K.M. Smith for providing instrument time at the UC Davis crystallographic facility.

References and Notes

1. (a) Kurreck, H.; Huber, M. *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 849. (b) Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435.
2. (a) Jang, H. G; Cox, D. D.; Que, L., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 9200. (b) Funabiki, T.; Ishikawa, M.; Nagai, Y.; Yorita, J.; Yoshida, S.; *J. Chem. Soc., Chem. Commun.* **1994**, 1951. (c) Koch, W. O.; Krueger, H.-J. *Angew. Chem. Int. Ed. Engl.* **1996**, *34*, 2671. (d) Bianchini, C.; Frediani, P.; Laschi, F.; Meli, A.; Vizza, F.; Zanello, P. *Inorg. Chem.* **1990**, *29*, 3402. (e) Matsuura, T.; Matsushima, H.; Kato, S.; Saito, I. *Tetrahedron* **1972**, *28*, 5119.
3. Belostotskaya, I. S.; Komissarova, N. L.; Dzhuaryan, E. V.; Ershov, V. V. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1972**, 1594.
4. (a) A crystal structure determination showed no significant distortion of the aryl ring in **3**. Crystal data **3:** $C_{16}H_{26}O_2$, FW = 250.37, T = 118 K, Cu Kα radiation, λ = 1.54178 Å, triclinic, P $\bar{1}$, a = 5.917(2) Å, b = 9.832(2) Å, c = 13.409(3) Å, α = 82.11(2)°, β = 78.46(2)°, γ = 79.93(2), V = 748.3(3) Å^3, Z = 2, ref F^2, R_1 ($I>2\sigma(I)$) = 0.0480, wR2 (all data) = 0.1248. (b) Complete data have been deposited with the CCDC.
5. Rieche, A.; Gross, H.; Höft, E. *Chem. Ber.* **1960**, *93*, 88.
6. Lindsey, J. S.; Schreiman, L. C.; Hsu, H. C.; Kearney, P. C.; Marguerettaz, A. M. *J. Org. Chem.* **1987**, *52*, 827.
7. Lindsey, J. S.; Wagner, R. W. *J. Org. Chem.* **1987**, *54*, 828.
8. Crystal data **10:** $C_{52}H_{44}N_4O_3{\bullet}CH_2Cl_2$, FW = 857.84, T = 126 K, Cu Kα radiation, λ = 1.54178 Å, monoclinic, C2/c, a = 24.581(12) Å, b = 10.684(5) Å, c = 33.97(2) Å, β = 108.64(4)°, V = 8454(7) Å^3, Z = 8, ref. F^2, R_1 ($I>2\sigma(I)$) = 0.0906, wR2 (all data) = 0.2861.[4b]
9. Speier, G.; Tyeklar, Z. *Chem. Ber.* **1979**, *112*, 389.
10. NMR ($CDCl_3$), mass spectrometric and mp data are as follows: **9:** ^{1}H NMR: (500 MHz) δ 9.22 (*d*, 2H; H3, H7), 8.97 (d, 2H; H2, H8), 8.84 (*AB*, 4H; H12, H13, H17, H18), 8.33-11 (m, 6H; *o*-phenyl-H), 7.83-71 (m, 9H; m, *p*-phenyl-H), 7.47 (s, 1H), 1.19 (s, 9H, *t*-butyl), 0.78 (s, 9H, *t*-butyl), -2.68 (s, 2H; NH) ppm; ^{13}C NMR: (126 MHz) δ 185.24, 181.71, 148.98, 147.90, 143.42, 142.66, 141.83, 141.58, 134.52, 134.44, 134.35, 127.95, 127.89, 126.83, 126.80, 126.74, 121.09, 120.64, 117.73, 37.88, 34.72, 31.17, 29.11 ppm; HRMS: calc. 758.36208, found 758.36227 as pyrocatechol; mp 78–81 °C (dec.) **10:** ^{1}H NMR: (500 MHz) δ 9.12 (bs, 2H; H3, H7), 8.95 (d, 2H; H2, H8), 8.84 (bs, 4H; H12, H13, H17, H18), 8.35-08 (m, 6H; *o*-phenyl-H), 7.83-70 (m, 9H; *p*-phenyl-H), 7.17 (s, 1H), 1.21 (s, 9H, *t*-butyl), 0.79 (s, 9H, *t*-butyl), -2.79 (s, 2H; NH) ppm; ^{13}C NMR: (126 MHz) δ 163.84, 162.28, 147.24, 141.84, 141.59, 141.46, 136.78, 134.55, 134.47, 134.33, 127.92, 127.87, 126.80, 126.72, 121.24, 120.57, 112.69, 37.58, 36.15, 30.45, 28.99 ppm; HRMS: calc. 772.34134, found 772.34160; mp 260–62 °C. **11:** ^{1}H NMR: (500 MHz) δ 9.59 (d, 2H; H3, H7), 8.92 (d, 2H; H2, H8), 8.83 (*AB*, 4H; H12, H13, H17, H18), 8.40-01 (m, 6H; *o*-phenyl-H), 7.84-68 (m, 9H; m, *p*-phenyl-H), 7.50 (s, 1H), 1.44 (s, 9H, *t*-butyl), 0.85 (s, 9H, *t*-butyl), -2.79 (s, 2H; NH) ppm; ^{13}C NMR: (126 MHz) δ 213.42, 205.30, 156.85, 141.91, 141.62, 135.72, 134.46, 127.90, 126.78, 126.73, 126.70, 121.51, 120.83, 113.05, 45.67, 43.71, 27.08, 26.33 ppm; HRMS: calc. 732.34643, found 732.34621; mp 248–50 °C.

(*Received in USA* 11 *August* 1997; *accepted* 10 *September* 1997)