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A SYNTHESIS FOR P-QUINOL COMPOUNDS FROM PHENOLS FUSED WITH OTHER SATURATED RINGS

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Abstract
Starting with a bicyclic or steroidal phenol, a p-quinol compound has been synthesized without side-products with use of a photosensitizer.

A lot of work has been done on the photosensitized oxygenation of phenols (1). Mostly the phenols had been highly substituted by tert. butyl groups.

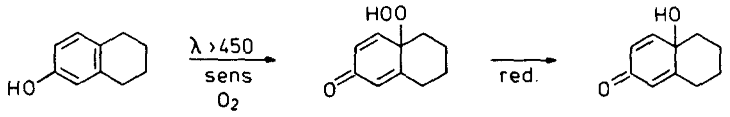
In the majority of these experiments a para-unsubstituted phenol was used. If a para-substituent was present, a hydroperoxide was formed as primary product, which underwent secondary reactions. As far as we know, photosensitized oxygenation of polycyclic compounds with a phenolic ring fused with other saturated rings has never been reported.

We recently found that such a compound yielded quantitatively a rather stable hydroperoxide upon photosensitized oxygenation. The hydroperoxide could easily be converted into the p-quinol. It seems probable that estrone and estradiol will react in the same way. Without light the p-quinol from estrone has been synthesized in low yield in the presence of side-products (2).

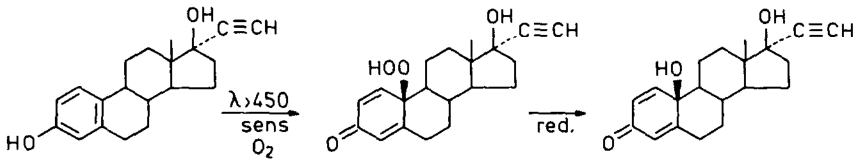
The experiments were performed with two compounds: 5,6,7,8 tetrahydro-2-naphtol (I) and ethinylestradiol (IV), a frequently used estrogenic steroid in the contraceptive pill. With another photosensitizer, methylene blue, the same products (II and IV) have been obtained. The reactions were carried out in mixtures (3 : 7) of methanol and phosphate buffer (pH 7.4), the optimal conditions for hematoporphyrin (8×10^{-5} M) to act as photosensitizer (3). During the reaction the solution was oxygenated.

A 1% K_2CrO_4 filter was used to eliminate wavelengths below 450 nm preventing direct decomposition of the initial compounds and of the products (4) by UV light. A vessel (Ø 34 mm) with 150 ml solution of hematoporphyrin and substrate (2.5×10^{-4} M) was placed at a distance of 40 cm from the lamp (a 1000 Watt Hg Xe lamp, model 6295, Oriel Co.). The conversion could be followed by HPLC (5 RP-2, 150 x 4.6 mm ID, methanol/water = 54/46, UV detection beneath 240 nm): the analysis time was 5 minutes. After total conversion (within 2 hours) the methanol was evaporated. Compound II was easily extracted with ethylacetate and compound V with diethylether. With NaI the initially formed hydroperoxides were reduced directly to the corresponding alcohols III and VI.

The products II, III, V and VI have been identified by their UV, IR, NMR, CD and MS spectral data as compared with those of p-quinol compounds described in literature (2, 5, 6).



I II III



IV V VI

The NMR signal of the C_{18} methyl group (5) and the CD spectrum (6) indicate that from VI only the 10-β substituted stereoisomer has been formed.

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