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# The Stereochemistry of Adduct Formation between a Lignin Model Quinone Methide and Anthrone, 10-Methylanthrone and 10-Phenylanthrone

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**Anthrone, 10-methylanthrone and 10-phenylanthrone reacted with the quinone methide derived from a phenolic lignin model compound, [1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-1-propanol], forming adducts similar to those believed to be intermediates in anthraquinone accelerated delignification reactions. Both *threo* and *erythro* isomers were obtained for the anthrone and 10-methylanthrone adducts. The reactions are assumed to be thermodynamically controlled; the *threo* isomer is formed faster. The stereochemistry of the 10-phenylanthrone adduct could not be resolved on the basis of the NMR spectra recorded.**

The catalytic delignification of wood by anthraquinone (AQ) is attributed,[1,2] to the transient adduct formation between lignin quinone methides and reduced species of AQ, mainly anthrahydroquinone (AHQ). As a consequence of a heterolytic fragmentation these adducts are cleaved at their β-ether bonds and AQ is regenerated. However, some AQ is lost during the cooking.[3,4] The disappearance of AQ has been believed to be due to formation of irreversible linkages[5] between lignin quinone methides and anthrone (AN),[6] the second reduction product of AQ. However, AN has also proved to be effective in cleaving β-ether bonds of model compounds under soda cooking conditions.[7,8]

The accelerating effect of AQ in delignification reactions has also been explained by a single-electron transfer mechanism,[9,10] in which AHQ transfers electrons, without forming bonds, to the reactive lignin quinone methides, causing them to fragment.

Adduct formation between lignin model quinone methides derived from phenolic compounds and various nucleophiles has been reported to be stereoselective. Predominantly *threo* isomers have been obtained in reactions of quinone methides with amines,[11] and with water[12] in dioxane solution, and exclusively *threo* adducts have been obtained with AHQ and AN in aqueous solutions.[13] The *threo* structure has been proved through chemical reactions, NMR spectroscopy and X-ray analysis.[14,15] In contrast, both *threo* and *erythro* isomers have been obtained[16] in reactions between trimethylsilyl ethers of AHQ and AN with non-phenolic lignin model compounds. In these reactions a quinone methide cannot be formed and the reaction proceeds *via* a carbocation intermediate. The decreased stereoselectivities were assumed to be due to the more reactive carbocation.[11] It has been postulated[11] that carbocations also are intermediates in reactions of quinone methides with

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water in the presence of catalytic amounts of HCl. The ratio of *erythro* and *threo* isomers in these reactions was approximately 1:1.[12]

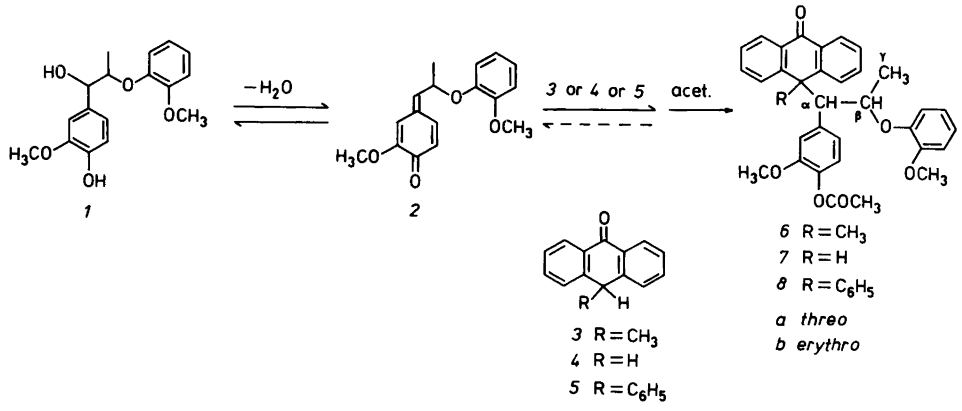
In reactions of carboxylic acids[12] with quinone methides the preference for *erythro* adducts has been attributed to solvation effects.[11]

In the course of a study on the effect of anthrone and its derivatives on the rate of cleavage of β-ether bonds in lignin model compounds, we prepared some anthrone and substituted anthrone adducts.[17] Now we have continued the study of the reaction of lignin quinone methides with anthrone and its C-10 substituted derivatives in alkaline aqueous solution. Both the *erythro* and *threo* adducts were obtained. The *erythro-threo* ratio was increased by extending the reaction time and placing a larger substituent at C-10 in the anthracenyl ring.

## RESULTS AND DISCUSSION

*10-Methylanthrone adducts.* In a previous article[17] we reported the reaction between 10-methylanthrone *3* and the quinone methide *2* derived from the phenolic lignin model compound *1*, 1-(4-hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-1-propanol, in alkaline aqueous solution. After acetylation, the *threo* adduct *6a* [1-(4-acetoxy-3-methoxyphenyl)-1-(9-oxo-10-methyl-9,10-dihydro-10-anthryl)-2-(2-methoxyphenoxy)propane] was obtained, as revealed by its characteristic $^1$H NMR spectrum, together with an unidentified product.[17] The product has now been identified as the *erythro* isomer *6b* on the basis of NMR spectra. The observed α,β-coupling constant in the $^1$H NMR spectrum is small ($J$ 2.7 Hz, indicating a dihedral angle of 60°) compared with the corresponding coupling constant of the *threo* isomer ($J$ 10 Hz). And, as is typical for *erythro* isomers,[16] the signal of the methoxyl group ($\delta$ 3.63) in the α-aryl substituent is less highly shielded than the corresponding signal of the *threo* isomer ($\delta$ 3.40). The upfield shift of the methoxyl signal of the β-substituent ($\delta$ 3.69 for *6b*, $\delta$ 4.00 for *6a*) has also been observed for other *erythro* adducts.[16] The differences in chemical shifts of the two isomers are far less in $^{13}$C NMR spectra than in $^1$H NMR spectra (Experimental).

*Reaction time.* To test if reaction time has any effect on the *erythro-threo* ratio, the chloroform solutions of quinone methide *2* were added to the alkaline aqueous solutions of




*Scheme 1.* Adduct formation between a lignin quinone methide and anthrone, 10-methylanthrone and 10-phenylanthrone.

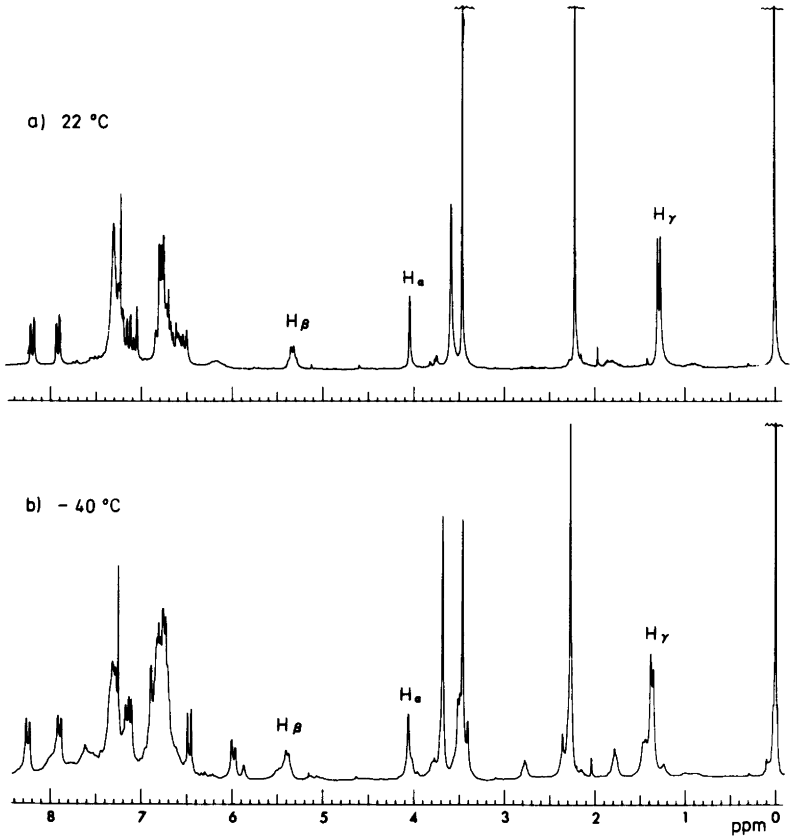



*Fig. 1.* 200 MHz $^1$H NMR spectra of *8* recorded (a) at 22 °C and (b) at −40 °C.

anthrone and 10-substituted anthrones for longer reaction times than in the earlier reported method.[13] Increasing the reaction time from 20 min to 40 min in the case of *3* increased the *erythro-threo* ratio of the isolated isomers of *6* from 0.8 to 1.0, and the combined yields rose from 32 % to 49 %. When the addition time of *2* to the alkaline solution of AN *4* was increased from 18 min to 1 h 15 min the ratio of *erythro* to *threo* isomer (*7b*/*7a*) increased from 0.2 to 0.7, as estimated from the characteristic methoxyl signals in the $^1$H NMR spectrum of the crude, non-acetylated reaction mixture (200 MHz, $\delta$ 3.35 and $\delta$ 4.00 for *7a* and $\delta$ 3.78 and $\delta$ 3.85 for *7b*). These results can be explained by kinetic and thermodynamic control of the reaction. Under the chosen conditions the *threo* isomer is formed faster and the *erythro* isomer is formed under thermodynamic control, and the equilibrium is reached faster when the proton at C-10 is replaced by a larger group. The exclusive formation of *threo* isomer *7a* obtained by others [13] can be explained by the short reaction time used (5−10 min). In contrast, in the $ZnBr_2$ catalyzed isomerization of a non-phenolic adduct the *threo* isomer has been found more stable.[16]

*10-Phenylanthrone adducts.* To elucidate the dependence of the structure of an adduct on the thermodynamic equilibrium, adduct *8* with a large 10-substituent was prepared. In a reaction between *2* and 10-phenylanthrone *5*, adduct *8* was obtained in 31 % yield after acetylation and purification. According to TLC it was a single isomer. The $^1$H NMR

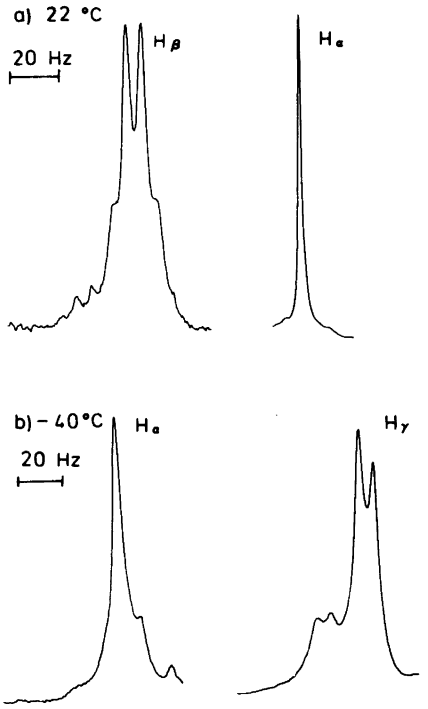



*Fig. 2.* Five-fold expansions of some protons of the $^1$H NMR spectra of *8* recorded (a) at 22 °C and (b) at −40 °C.

spectrum recorded at +22 °C revealed no coupling between α- and β-protons. The H-α signal (δ 4.05) is a singlet and the H-β signal (δ 5.34) is a quartet (Figs. 1a and 2a). This could be explained by a locked conformer in which the dihedral angle between α- and β-protons is 90° and which leads to a coupling constant of zero. It was expected that lowering the probe temperature would reveal a spectrum of two different conformers and some coupling between α- and β-protons. And indeed, in the spectrum recorded at −40 °C (Figs. 1b and 2b) the two doublets of H-γ (*J* of both is 5.6 Hz) clearly reveal the existence of two conformers of *8*. Irradiation of H-β gave two singlets. Moreover, as can be seen from Figs. 1b and 2b, there is a shoulder in the signal of H-α. Evidently it is part of the doublet of H-α of the minor conformer, the other part then being hidden under the "singlet". The predominance of the conformer with no α,β-coupling was unexpected and has not been explained. On analogy with the values obtained for *6b*, *7b* and other AN-adducts,[16] the small difference in the chemical shifts of the two aromatic methoxyl groups (δ 3.47 and δ 3.59) in the $^1$H NMR spectrum would suggest *erythro* structure. However, it is impossible to resolve the stereochemistry of adduct *8* on the basis of the recorded NMR spectra ($^1$H NMR and $^{13}$C NMR, Experimental) because replacement of the proton at C-10 by the large phenyl group can affect dramatically the chemical shifts and cause upfield shift of the methoxyl protons of the β-substituent. Such an upfield shift has been reported[13] for some adducts having a methoxyl or an acetoxy group at the 10-position.

In summary, the successful synthesis of adducts *6* and *8* with both a γ-substituent and a large 10-substituent indicates that the steric crowding is not so severe as thought earlier.[15] Interestingly, both *threo* and *erythro* isomers were obtained for *6* and *7* under alkaline aqueous conditions. Earlier[13] only *threo* adducts have been observed in similar reactions.

The formation of *erythro* adducts during longer reaction times is attributed to thermodynamic control of the reaction.

## EXPERIMENTAL

Melting points, determined in open capillary tubes with an electrothermal apparatus, are uncorrected. $^1$H NMR spectra were recorded on Jeol JNM–PMX 60 and Jeol JNM–FX200 FT spectrometers and $^{13}$C NMR spectra on a Jeol JNM PFT 100 spectrometer for solutions in deuteriochloroform. Mass spectra were obtained with a Jeol JMS–01SG-2 instrument. All acetylations were performed with a mixture of dry acetic anhydride and pyridine (1:1).

### Starting materials

*1-(4-Hydroxy-3-methoxyphenyl)-2-(2-methoxyphenoxy)-1-propanol* 1[18] was obtained as a mixture of *erythro* and *threo* isomers (9:1).[19]

*10-Methylanthrone* 3: for preparation and spectral data see Ref. 17 and references therein.

*10-Phenylanthrone* 5 (10-Phenyl-9-(10H)anthracenone) was synthesized by the previously reported method.[20] $^1$H NMR (60 MHz): $\delta$ 5.48 (1 H, s, 10(C)–H), 7.17–7.73 (11 H, m, ArH), 8.37–8.60 (2 H, m, ArH). MS [75 eV; m/e (% rel. int.)]: 271 (27.2), 270 ($M^+$, 100.0), 241 (24.7), 239 (38.4), 193 (26.8), 165 (38.2), 120 (28.8), 69 (31.9), 44 (60.0).

*Adducts* were prepared by Landucci's method[13] at 35–40 °C, with the reaction time varied between 18 min and 1 h 15 min.

threo-*1-(4-Acetoxy-3-methoxyphenyl)-1-(9-oxo-10-methyl-9,10-dihydro-10-anthryl)-2-(2-methoxyphenoxy)propane* 6a[17] was obtained by allowing the quinone methide of *1* (304.0 mg, 1.0 mmol) to react with 10-methylanthrone (187.2 mg, 0.9 mmol) according to the published method.[13] Chromatography of the crude, acetylated mixture twice on silica dry-column (Woelm Pharma GmbH & Co; chloroform; cyclohexane-ethyl acetate-chloroform 4:1:2) gave *6a* in 18 % yield (87.8 mg) and

erythro-*1-(4-acetoxy-3-methoxyphenyl)-1-(9-oxo-10-methyl)-9,10-dihydro-10-anthryl)-2-(2-methoxyphenoxy)propane* 6b in 14 % yield (67.4 mg), when the reaction time was 20 min. Increasing the reaction time to 40 min increased the combined yield to 49 % (*6a* 25 %, *6b* 24 %). *6b*: m.p. 75–79 °C (subl.), $^1$H NMR (200 MHz): $\delta$ 0.79 (3 H, d, $J$ 6.1 Hz, H-$\gamma$), 2.01 (3 H, s, 10-$CH_3$), 2.31 (3 H, s, $COCH_3$), 2.77 (1 H, hump, H-$\alpha$), 3.63 (3 H, s, $OCH_3$), 3.69 (3 H, s, $OCH_3$), 4.21 (1 H, dq, $J$ 2.7 Hz, $J$ 6.1 Hz, H-$\beta$), 6.30 (1 H, d, $J$ 8.5 Hz, ArH), 6.70–6.88 (5 H, m, ArH), 7.07 (1 H, s, ArH), 7.35–7.40 (6 H, m, ArH), 8.16 (2 H, m, ArH). Assignments were confirmed by selective irradiation. $^{13}$C NMR (25.15 MHz): $\delta$ 18.5 (C-$\gamma$), 20.7 (acetate $CH_3$), 23.4 ($CH_3$), 46.2 (C-10), 55.7 (2×$OCH_3$), 67.4 (C-$\alpha$), 72.8 (C-$\beta$), 111.8–150.3 (aromatic carbons), 168.6 (acetate CO), 184.3 (CO). MS [18 eV; m/e (% rel. int.)]: 536 ($M^+$, 5.3), 330 (21.4), 329 (92.2), 287 (12.6), 209 (37.0), 208 (100.0), 207 (30.2), 206 (68.1), 165 (18.8), 164 (84.5), 163 (52.2), 124 (68.2), 123 (27.5), 109 (16.5). Mol. wt., obs. 536.2196, calc. for $C_{34}H_{32}O_6$ 536.2198.

*1-(4-Acetoxy-3-methoxyphenyl)-1-(9-oxo-10-phenyl-9,10-dihydro-10-anthryl)-2-(2-methoxyphenoxy)propane* 8 was prepared by adding the chloroform solution of the quinone methide *2* derived from *1* (608.0 mg, 2.0 mmol) to the alkaline solution of 10-phenylanthrone (486.0 mg, 1.8 mmol) during a period of 45 min according to the published procedure.[13] Chromatography of the crude acetylated product on a silica dry column (Woelm Pharma GmbH & Co; cyclohexane – ethyl acetate – chloroform, 4:1:2) gave a light yellow solid product in 31 % yield (without optimizing). Recrystallization from ethanol gave white needles, m.p. 131–140 °C, and from acetone-pentane m.p. 150–154 °C. $^1$H NMR (200 MHz, +22 °C): $\delta$ 1.29 (3 H, d, $J$ 6.1 Hz, H-$\gamma$), 2.22 (3 H, s, $COCH_3$), 3.47 (3 H, s, $OCH_3$), 3.59 (3 H, s, $OCH_3$), 4.05 (1 H, s, H-$\alpha$), 5.34 (1 H, q, $J$ 6.1 Hz, H-$\beta$), 6.19–8.23 (20 H, m, ArH). Assignments were confirmed by selective irradiation. $^{13}$C NMR (25.15 MHz): $\delta$ 19.0 (C-$\gamma$), 20.7 (acetate $CH_3$), 55.2 (2×$OCH_3$), 56.0 (C-10), 60.0 (C-$\alpha$), 71.0 (C-$\beta$), 111.1–157.3 (aromatic carbons), 168.7 (acetate CO), 183.4 (CO). MS [19 eV; m/e (% rel.

int.)]: 598 ($M^+$, 8.4), 329 (14.5), 286 (11.6), 272 (10.4), 271 (34.3), 270 (100.0), 269 (49.4), 252 (16.5), 239 (12.0), 206 (19.1), 165 (13.9), 164 (37.4), 163 (19.7), 132 (33.3), 125 (19.8), 124 (84.6), 91 (16.6). Mol. wt., obs. 598.2328, calc. for $C_{39}H_{34}O_6$ 598.2353.

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