Photochemical Nucleophilic Substitution of Methoxy-benzoquinones and -naphthoquinones with Methylamine. Examples of Substitution Reactions following Different Thermal and Photochemical Pathways with High Regiospecificity

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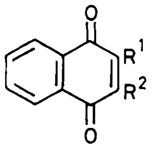
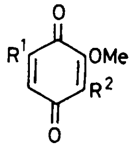
Summary Thermally and photochemically induced substitution reactions between 2-methoxy-1,4-naphthoquinone and methylamine follow different pathways with high regiospecificity: thermal reaction results in replacement of the 2-methoxy group by the amine, whereas photosubstitution involves replacement of hydrogen at the 3-position; 2,6-dimethoxy-1,4-benzoquinone shows a similar behaviour.



(1)

a; R^1=OMe, R^2=H
b; R^1=NHMe, R^2=H
c; R^1 = OMe, R^2 = NHMe



(2)

a; R^1=OMe, R^2=H
b; R^1=NHMe, R^2=H
c; R^1=R^2=NHMe
d; R^1=OMe, R^2=NHMe

ALTHOUGH photochemically induced nucleophilic substitution reactions of quinone systems are well documented,[1-3] in all cases the substituent replaced is attached to an aromatic ring annelated to the quinone residue. Thermal replacement of substituents attached directly to the quinonoid ring is well known,[4] but corresponding photochemical reactions have not been observed. To examine the feasibility of the latter reactions, the photochemical reactivities of 2-methoxy-1,4-naphthoquinone (**1a**) and 2,6-dimethoxy-1,4-benzoquinone (**2a**) towards methylamine have been investigated.

Nucleophilic substitution of 2-methoxy-1,4-naphthoquinones occurs by Michael addition, followed by elimination of the methoxy substituent. If such reactions were charge controlled, simple frontier orbital considerations suggest that in the ground state (LUMO controlled), attack by the nucleophile would be favoured at the methoxy-bearing carbon atom, whereas in the first excited state (HOMO controlled) attack would occur preferentially at the unsubstituted position.† More detailed PPP–MO calculations for (**1a**) and (**2a**)‡ show that in the first π, π^* excited singlet state there is a significantly larger decrease in electron density at the 3-position than the 2-position, again

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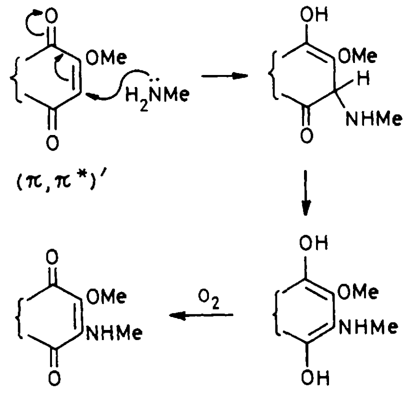
† The ground state reaction is more likely to be controlled by the relative stabilities of the two intermediate anionic addition complexes, but simple resonance considerations for these structures also predict preferred attack at the methoxy-bearing carbon atom.

‡ For parameters used see reference 3.

suggesting that in a charge controlled reaction, photochemical attack would be favoured at position 3. This possible dichotomy of thermal and photochemical behaviour for (**1a**) and (**2a**) was thus investigated.

Thermal reaction between 2-methoxy-1,4-naphthoquinone (**1a**) and methylamine was highly specific and gave exclusively the 2-methylamino-derivative (**1b**).[5] At temperatures below −40 °C the thermal reaction could be effectively suppressed. U.v. irradiation of a solution of (**1a**) in dichloromethane containing methylamine at −45 °C ($\lambda > 320$ nm) gave exclusively the 2-methoxy-3-methylamino-derivative (**1c**), isolated in 66% yield. No other products were detected by t.l.c. Thus it can be concluded that photochemical addition of methylamine occurs at the 3-position with high regiospecificity, whereas thermal addition occurs at the 2-position with an equally high regiospecificity. The probable sequence of steps involved in the photochemical formation of (**1c**) is summarised in the Scheme.



Scheme

At −45 °C under aerobic conditions the quantum yield of the reaction in dimethylformamide was 0·36 over the wavelength range 300—430 nm (degassing the solution had little effect). Unlike 1,4-naphthoquinone itself, which shows a well resolved $n \rightarrow \pi^*$ band and is photochemically unreactive towards methylamine, (**1a**) shows only a near-u.v. $\pi \rightarrow \pi^*$ band, thus suggesting that a (π,π^*) state is implicated in the reaction. In the presence of benzophenone the reaction of (**1a**) with methylamine was inhibited by an amount corresponding to the filter effect of the former compound. The energy of the lowest triplet state of (**1a**) is *ca.* 280 kJ mol^{-1} (as indicated by its phosphorescence spectrum), and is below that of benzophenone (290 kJ mol^{-1}) and thus triplet energy transfer from the latter compound should be efficient. The absence of any sensitising effect suggests that the reaction occurs from the first (π,π^*) singlet state of (**1a**).

2,6-Dimethoxy-1,4-benzoquinone (**2a**) was investigated in a similar manner to (**1a**). Thermal reaction with methylamine was rapid, and gave initially 2-methoxy-6-methylamino-1,4-benzoquinone (**2b**),§ which readily reacted further to give the known[6] bismethylamino-compound (**2c**). Irradiation of dichloromethane solutions of (**2a**) containing methylamine at −40 °C gave a different product, which was isolated in 33% yield, and was identified as 2,6-dimethoxy-3-methylamino-1,4-benzoquinone (**2d**).§

T.l.c. analysis of the mixture showed the presence of (**2d**) and unchanged (**2a**) only. Thus (**2a**) shows the same highly specific diversity of thermal and photochemical behaviour as (**1a**).

The quantum yield of the reaction in dimethylformamide (aerobic) at −45 °C was 0·16 (300—430 nm). Again no triplet sensitisation by benzophenone was observable [E_T for (**2a**) *ca.* 250 kJ mol^{-1} as indicated by its phosphorescence spectrum]. Like (**1a**), (**2a**) shows only a $\pi \rightarrow \pi^*$ band in the near-u.v. region. As 1,4-benzoquinone itself is photochemically unreactive towards amines, and shows a well resolved $n \rightarrow \pi^*$ band, this precludes a possible mechanism for photosubstitution involving electron abstraction from the amine by photoexcited quinone, followed by combination of the resultant radical ions,[2] and favours a mechanism involving direct addition of the amine to the quinone in its π,π^* excited state (Scheme).

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§ New compounds gave mass spectrometric, i.r., ^{1}H n.m.r., and microanalytical data consistent with the assigned structures.

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