Photochemical Nucleophilic Substitution of 5,8-Dimethoxy-1,2-dimethylnaphth-[2,3-*d*]imidazole-4,9-dione. An Unusual Long-range Directing Effect in the Photoexcited State

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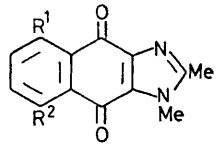
Summary Photochemical substitution of 5,8-dimethoxy-1,2-dimethylnaphth[2,3-*d*]imidazole-4,9-dione (**1a**) with primary alkylamines gives mixtures of the 5-alkylamino-8-methoxy- and 8-methylamino-5-methoxy-isomers in high yield; the predominance of the 5-alkylamino-isomers, which is not observed in the thermal substitution reaction, can be explained in terms of the predicted π-electron densities at the 5- and 8-positions in the first excited state.

Photochemical nucleophilic substitution in aromatic systems often differs appreciably from the corresponding thermal reactions, particularly in the case of substituent directing effects.[1] If the photoreaction has a negligible activation energy, directing effects may be governed largely by the π-electron density in the excited state, and consequently the photochemical process may show an enhanced substituent sensitivity. This was observed for photosubstitution of 5-nitro- and 6-nitro-2,3-dimethoxynaphthalenes with hydroxide anion, where the nitro-groups had a pronounced influence on the course of the methoxide displacement reaction, despite their remoteness from the reaction centre.[2] The observed 'extended meta-activation' was explicable in terms of the computed π-electron densities at the 2- and 3-positions. Unfortunately, information concerning the thermal replacement reactions was not provided, and the peculiarity of the long-range directing effect to the photoreaction cannot be adduced. We now report the substitution reactions of a dimethoxy-quinone system with amines, in which the photochemical process shows a pronounced long-range substituent effect not observed in the thermally induced reaction.

The susceptibility of methoxyanthraquinones towards photochemical nucleophilic substitution has been noted previously,[3,4] and to test the generality of this synthetically useful procedure, we have examined the related heterocyclic system (**1a**). 5,8-Dimethoxy-1,2-dimethylnaphth-[2,3-*d*]imidazole-4,9-dione (**1a**)† gave no reaction with methylamine in dichloromethane at room temperature, but on exposure to near-u.v. light ($\lambda > 320$ nm) an intense purple colour developed. Preparative t.l.c. (silica, CH_2Cl_2) afforded starting material and two isomeric dark red compounds in 83% combined yield, no other products being detectable. The photoreaction with cyclohexylamine proceeded similarly to give two isomeric mono-substituted products in 78% yield.

Mass spectra and elemental analysis indicated structures (**1b**) and (**1c**), and (**1d**) and (**1e**) for the products from methylamine and cyclohexylamine, respectively. Structural differentiation between each pair of isomers was made on the basis of i.r. and visible absorption spectra,‡ the products having the following properties [structure, m.p., λ_{max} (C_6H_{12})]: (**1b**), 206—208 °C, 536 nm; (**1c**), 198—200 °C, 528 nm; (**1d**), 226—228 °C, 541 nm; and (**1e**), 210—211 °C, 539 nm. Quantitative analysis of the reaction products (prep. t.l.c.) from methylamine and cyclohexylamine showed in both cases a predominance of the 5-alkylamino-isomer, *i.e.* (**1b**) : (**1c**) = 1·75 : 1, (**1d**) : (**1e**) = 1·80 : 1. The significantly greater reactivity of the 5-position of (**1a**) relative to the 8-position is surprising in view of the remoteness of the imidazole ring from the reaction centre and the insulating effect of the carbonyl groups.



(1)

a; $R^1 = R^2 = MeO$
b; $R^1 = MeNH, R^2 = MeO$
c; $R^1 = MeO, R^2 = MeNH$
d; $R^1 = C_6H_{11}NH, R^2 = MeO$
e; $R^1 = MeO, R^2 = C_6H_{11}NH$
f; $R^1 = MeNH, R^2 = H$
g; $R^1 = H, R^2 = MeNH$

To see if a similar directing effect operated in the ground state, the thermal reaction of (**1a**) with amines was examined. Thermal substitution proved to be extremely inefficient and only slow decomposition occurred when (**1a**) was heated with benzene or ethanol solutions of the amine at temperatures ranging from 80 to 180 °C. Discrete substitution products were observed only on heating (**1a**) to reflux in pure cyclohexylamine, when (**1d**) and (**1e**) were formed together with several secondary reaction products. Analysis of the reaction mixture after 25 min showed an isomer distribution (**1d**) : (**1e**) of *ca.* 3 : 1. However, this distribution does not necessarily reflect the relative rates of formation of the two isomers, as they suffer extensive secondary decomposition during the reaction, possibly at different rates.

To examine this, an equimolar mixture of (**1d**) and (**1e**) was heated in cyclohexylamine for a similar period of time. Decomposition of both isomers occurred, giving an isomer distribution (**1d**) : (**1e**) *ca.* 3 : 1. Clearly the 8-isomer (**1e**) decomposes more rapidly than (**1d**), and the unequal isomer distribution found in the thermal substitution of (**1a**) is due solely to this fact. Thus (**1a**) gives (**1d**) and (**1e**) in the thermal substitution reaction at approximately equal rates. In summary, then, the photochemical reaction is far superior to the thermal reaction as a preparative procedure, particularly as the former gives no secondary products, and the photoreaction is peculiar in showing a pronounced

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† All new compounds were characterised by elemental analysis and mass spectrometry.

‡ The structures of several 5- and 8-alkylamino-1,2-dimethylnaphth[2,3-*d*]imidazole-4,9-diones have been established by unambiguous synthesis, and in all cases the carbonyl region permits a ready distinction between the isomeric forms (ref. 5).

difference in the relative reactivities of the 5- and 8-positions.

The photosubstitution reactions may involve direct attack by the amine on the excited state of (**1a**) to give an addition complex, which then eliminates methoxide ion. Alternatively, the excited state of (**1a**) may abstract an electron from the amine to form a radical anion–radical cation pair which would combine to give the same intermediate. Although it is difficult to distinguish between these two processes, the latter appears to be unlikely in view of the fact that (**1a**) is photochemically unreactive towards secondary amines (*e.g.*, dimethylamine), which are better electron donors than primary amines. Most probably electron abstraction is a source of rapid deactivation of the excited state without overall substitution. Thus dimethylamine effectively quenched the reaction of (**1a**) with methylamine.

The reactions of (**1a**) with methylamine at 15 and −100 °C proceeded with equal facility, suggesting that the primary nucleophilic addition step has a negligible activation energy. Thus the directing effect of the imidazole ring may be due to an increased degree of electronic asymmetry in the excited state of (**1a**), rather than to any major differences in the transition state energies for the addition step.

Electron density changes in the excited state were evaluated by the PPP SCF-MO procedure, using empirically modified parameters.[5,6] The validity of the calculations was confirmed by the good agreement between the calculated and observed λ_{max} values for (**1a**—**c**) and for several other compounds in the same series [*e.g.*, λ_{max} (obs.), λ_{max} (calc.) (C_6H_{12}): (**1a**), 410 and 414; (**1b**), 536 and 538; (**1c**), 528 and 535; (**1f**), 513 and 517; and (**1g**), 509 and 509 nm]. A high degree of electronic symmetry was predicted for the ground state of (**1a**), with positions 5 and 8 having identical π-electron densities (0·944), whereas in the first excited state the 5-position was predicted to be more electron deficient than the 8-position (π-electron densities 0·808 and 0·817, respectively). Although small, these differences are significant, and may account for the different reactivities of the two positions. Thus in the excited state, the amine may attack the 5- and 8-positions at a rate determined largely by the magnitude of their partial positive charges, and thus the 5-substituted compound is produced most rapidly.

Long-range directing effects may prove to be a fundamental characteristic of many photosubstitution reactions, but unfortunately few systems are yet known that are suitable for testing this possibility. Methoxy-substituted quinones may prove to be most useful in this respect.

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