Further Evidence for the Regioselectivity Rules in Nucleophilic Aromatic Photosubstitution

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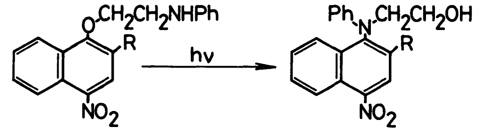
Synopsis. In order to assess the validity of our regioselectivity rules for nucleophilic aromatic photosubstitution, 4-nitronaphthyl ethers were designed and their photochemical behavior was studied by applying frontier molecular orbital theory. The results provide supporting evidence for our rules.

In a previous paper[1)] we proposed two rules to rationalize the regioselectivities observed in nucleophilic aromatic photosubstitutions; namely, (rule 1) photosubstitutions accompanying direct addition of a nucleophile to an excited aromatic substrate substituted with a strongly electron-withdrawing group (s) show HOMO-controlled regioselectivity, and (rule 2) those involving photoinduced electron transfer from a nucleophile to an aromatic substrate show LUMO-controlled regioselectivity, where, HOMO and LUMO, refer to those of the aromatic substrate in the ground state.

The objectives of the present paper are to extend the scope of application of these rules to naphthalene derivatives and, thus, to provide further evidence for the rules.

By analogy with the substituted benzenes previously reported to undergo photorearrangement,[2)] naphthalene derivatives **1** and **2** are designed and submitted to photoreaction.



1, R=H **3**, R=H
2, R=OMe **4**, R=OMe

HOMO-controlled Photosubstitution. Since 1-methoxy-4-nitro- and 1,2-dimethoxy-4-nitronaphthalenes can be regarded as simplified models for the nitroaromatic moieties of **1** and **2**, respectively, nucleophilic photosubstitutions of these model compounds were examined.

In Fig. 1a, the frontier electron density (FED) maps of the HOMO and LUMO of 1-alkoxy-4-nitronaphthalene are depicted. The values were calculated by the CNDO/2 approximation, assuming that the alkoxyl group can be replaced with a hydroxyl without causing any significant change in the FED distribution pattern.[1)] According to frontier molecular orbital theory, photosubstitutions are expected to occur at the carbons with high FED, *i.e.* C_1–OR, C_2 or C_4–NO_2. All the reactions so far reported (with cyanide, hydride as BH_4^-, and methoxide ions)[3)] have been observed at the position with the highest FED, C_4. Although the FED map in the LUMO suggests that the C_4-substitutions may also be interpreted as LUMO-controlled, electron transfer pathway cannot be expected for these nucleophiles, which have shown no tendency of electron release in the photosubstitutions of benzene derivatives.[1)]

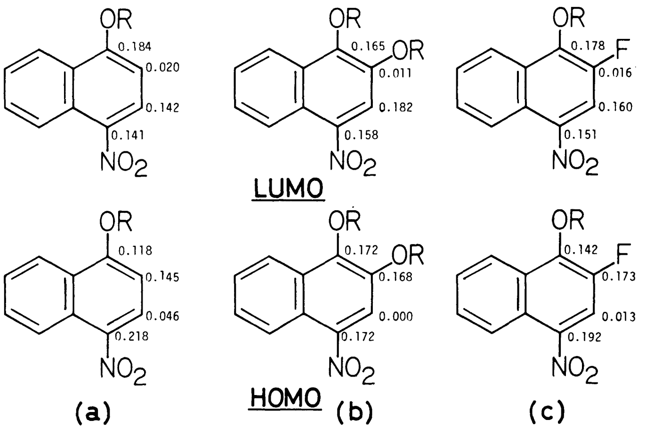


Fig. 1. Frontier electron density (FED) maps of the HOMO and LUMO of (a) 1-alkoxy-4-nitro-, (b) 1,2-dialkoxy-4-nitro-, and (c) 1-alkoxy-2-fluoro-4-nitronaphthalene.

The photoreaction of 1,2-dimethoxy-4-nitronaphthalene has not been reported, but for the present purpose we could adopt 2-fluoro-1-methoxy-4-nitronaphthalene as a good substitute, because the FED maps of the HOMO's and LUMO's of these two models show a similar pattern (Fig. 1b and 1c). Nucleophilic photosubstitutions of 2-fluoro-1-methoxy-4-nitronaphthalene have been reported to occur[4)] at C_1 with hydroxide ion, at C_2 with methoxide ion, and at C_4 with cyanide ion. A secondary reaction has been noted in the case of methoxide ion, replacing the nitro group at C_4 (an example of the photoreaction of the original model compound, 1,2-dimethoxy-4-nitronaphthalene). These three positions, C_1, C_2, and C_4, bear comparably large FED's (0.142, 0.173, and 0.192, respectively) and, therefore, the observed regioselectivity towards nucleophiles is consistent with rule 1.

LUMO-Controlled Photosubstitution. For the photoreactions accompanying electron transfer or the LUMO-controlled reactions, substitution in both **1** and **2** should occur at C_1 (intramolecular reaction at C_4 is sterically impossible) to afford rearranged products. On irradiating solutions of **1** and **2**, containing a catalytic amount of triethylamine, with a high-pressure Hg lamp, **3** and **4**, respectively, were isolated as reaction products in good yields (Eq. 1).[5)] It is also noticeable that the photosubstitution observed for **2** occurred only at C_1 and not at C_2; because the C_2 carbon is bonded to a good leaving group and its FED of the HOMO is sufficiently large to accept a nucleophile, the substitution should occur, at least partly, at this position if the reaction takes the HOMO-controlled pathway. This fact also underlines the importance of the LUMO in this photorearrangement. A marked contrast with the HOMO-controlled reactions strongly suggests that the rearrangements took place *via* electron transfer.

So far as we judge only by the structure of the product **3**, the observed regioselectivity of **1** is explicable either by rule 1 or rule 2, since its C_1 carbon has high FED's in both HOMO and LUMO. Rigorously speaking, it is difficult to rule out the HOMO-controlled mechanism. However, the LUMO-controlled pathway is more plausible, because even the nitroaromatic moiety with an additional electron-donating substituent, methoxyl group, in **2** is supposed to be able to accept an electron from the anilino moiety as discussed above and the counterpart in **1**, lacking in the methoxyl, is expected to have a larger electron affinity.

In order to obtain further supporting evidence for electron transfer process, we have tried to detect a transient species formed immediately after photoexcitation of **1** by means of nanosecond laser flash photolysis. However, it was found that the observation of transient spectra attributable to the charge-separated biradical consisting of the donor cation and acceptor anion was difficult due to strong fluorescence from the naphthalene moiety. Thus, no direct evidence for photoinduced electron transfer has been obtained.

Experimental

The details of the MO calculations have been described in a previous paper.[1)] ^{1}H-NMR Spectra were recorded on a Varian EM-390 spectrometer. Melting points are uncorrected. Homogeneity of the compounds was established by HPLC on a JASCO FLC-A10 using methanol as an eluent.

1-(2-Bromoethoxy)-4-nitronaphthalene. To a mixture of 3.82 g (20 mmol) of 4-nitro-1-naphthol[6)] and 9.30 g (50 mmol) of 1,2-dibromoethane in 15 ml of water containing 3 ml of dioxane was added a solution of 0.8 g (20 mmol) of sodium hydroxide in 10 ml of water under reflux with stirring during 1.5 h, and reflux was continued for 2 d. After cooling, the reaction mixture was poured into 30 ml of 5% aqueous sodium hydroxide solution and extracted with three 10-ml portions of dichloromethane. The extracts were collected and the solvent was removed by distillation. Chromatography on 80 g of active alumina eluting with benzene-dichloromethane mixture afforded 1.95 g (33%) of the bromide as yellow cyrstals: mp 77—78 °C; ^{1}H NMR ($CDCl_3$) δ=3.76 (2H, t, J=5 Hz, CH_2Br), 4.46 (2H, t, J=5 Hz, OCH_2), 6.63 (1H, d, J=9 Hz, H-2), 7.3—7.8 (2H, m, H-6 and H-7), 8.0—8.35 (2H, m, H-5 and H-8), 8.63 (1H, d, J=9 Hz, H-3).

Found: C, 48.72; H, 3.26; N, 4.97%. Calcd for $C_{12}H_{10}NO_3Br$: C, 48.67; H, 3.40; N, 4.73%.

1-(2-Bromoethoxy)-2-methoxy-4-nitronaphthalene. This compound was prepared from 2-methoxy-4-nitro-1-naphthol[7)] by a procedure similar to that described above for the bromide in a yield of 32%: mp 115—116 °C; ^{1}H NMR ($CDCl_3$) δ=3.71 (2H, t, J=6 Hz, CH_2Br), 4.02 (3H, s, OCH_3), 4.60 (2H, t, J=6 Hz, OCH_2), 7.4—7.7 (2H, m, H-6 and H-7), 8.17 (1H, s, H-3), 8.2—8.7 (2H, m, H-5 and H-8).

Found: C, 47.74; H, 3.71; N, 4.35%. Calcd for $C_{13}H_{12}NO_4Br$: C, 47.87; H, 3.71; N, 4.30%.

1-(2-Anilinoethoxy)-4-nitronaphthalene (1). This compound was prepared from aniline and the corresponding bromide by a reported procedure[2b)] in a yield of 59%: mp 161—162 °C; ^{1}H NMR ($CDCl_3$-DMSO-d_6) δ=3.5—3.8 (2H, m, CH_2N), 4.37 (2H, t, J=6 Hz, OCH_2), 5.56 (1H, t, J=5 Hz, NH), 6.2—7.2 (6H, m, C_6H_5 and H-2), 7.2—7.8 (2H, m, H-6 and H-7), 8.25—8.4 (2H, m, H-3 and H-8), 8.54 (1H, dd, J=2 and 8 Hz, H-5).

Found: C, 69.88; H, 5.00; N, 9.08%. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.08%.

1-(2-Anilinoethoxy)-2-methoxy-4-nitronaphthalene (2). This compound was prepared[2b)] from aniline and the corresponding bromide in a yield of 88%: mp 110.5—112 °C; ^{1}H NMR ($CDCl_3$) δ=3.60 (2H, t, J=5 Hz, CH_2N), 3.97 (3H, s, OCH_3), *ca.* 4.3 (1H, br s, NH), 4.43 (2H, t, J=5 Hz, OCH_2), 6.6—7.3 (5H, m, C_6H_5), 7.4—7.6 (2H, m, H-6 and H-7), 8.17 (1H, s, H-3), 8.15—8.3 (1H, m, H-8), 8.5—8.7 (1H, m, H-6).

Found: C, 67.18; H, 5.33; N, 8.02%. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28%.

1-[N-(2-Hydroxyethyl)anilino]-4-nitronaphthalene (3). The amine **1** (370 mg, 1.2 mmol) dissolved in a mixture of methanol (800 ml), acetonitrile (150 ml), and triethylamine (10 ml) was irradiated with a 400 W high-pressure Hg lamp for 50 min. Usual workup and chromatography on 50 g of silica gel eluting with a 1:1 mixture of benzene and dichloromethane afforded **3** (293 mg, 79%) as brick-red crystals: mp 131—132 °C; ^{1}H NMR ($CDCl_3$) δ=1.70 (1H, t, J=5 Hz, OH), 3.7—4.2 (4H, m, NCH_2CH_2O), 6.7—7.25 (5H, m, C_6H_5), 7.50 (1H, d, J=9 Hz, H-2), 7.4—7.8 (2H, m, H-6 and H-7), 8.01 (1H, dd, J=*ca.* 1.5 and 9 Hz, H-8), 8.31 (1H, d, J=9 Hz, H-3), 8.65 (1H, dd, J=*ca.* 1.5 and 9 Hz, H-5).

Found: C, 70.07; H, 4.95; N, 8.81%. Calcd for $C_{18}H_{16}N_2O_3$: C, 70.12; H, 5.23; N, 9.08%.

1-[N-(2-Hydroxyethyl)anilino]-2-methoxy-4-nitronaphthalene (4). Irradiation of the amine **2** under similar conditions to those used for **3** and usual workup afforded **4** as brick-red crystals in a yield of 53%: mp 117—118 °C; ^{1}H NMR ($CDCl_3$) δ=*ca.* 2.63 (1H, br t, J=*ca.* 5 Hz, OH), 3.75 (4H, br m, NCH_2CH_2O), 3.93 (3H, s, OCH_3), 6.45—7.2 (5H, m, C_6H_5), 7.35—7.6 (2H, m, H-6 and H-7), 7.7—7.9 (1H, m, H-8), 8.11 (1H, s, H-3), 8.4—8.6 (1H, m, H-5).

Found: C, 67.69; H, 5.54; N, 8.12%. Calcd for $C_{19}H_{18}N_2O_4$: C, 67.44; H, 5.36; N, 8.28%.

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5) For the solutions of *ca.* 10^{-4} mol dm^{-3}, the rearrangement occurred in more than 90% yields, as monitored by HPLC at 254, 300, and 350 nm. The yields described in Experimental are the results obtained in preparative scale, adopting higher concentrations and prolonged time of irradiation.

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