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Photoinduced Intramolecular Aromatic Nucleophilic Substitution (the Photo-Smiles Rearrangement) in Amino Ethers[1)]

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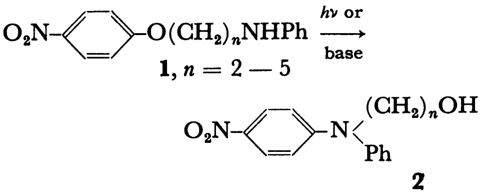
Intramolecular rearrangement was induced by light as well as base in a homologous series of 1-(*p*-nitrophenoxy)-ω-anilinoalkanes, *p*-$O_2NC_6H_4O(CH_2)_nNHPh$ (n=2—5), yielding *N*-(*p*-nitrophenyl)-ω-anilino-1-alkanols, *p*-$O_2NC_6H_4N(Ph)(CH_2)_nOH$. The reaction rate in acetonitrile showed abnormal order, $n=4>5>3>2$, which was reversed by the addition of triethylamine. The mechanism of this photorearrangement through a radical ion pair and a spiro type Meisenheimer complex was proposed. The anomaly in the reaction rate order was discussed on the basis of this mechanism.

The intramolecular nucleophilic aromatic substitution is generally called the Smiles rearrangement,[2)] which is in most cases induced by base. The reaction of the same type induced by light may be called the photo-Smiles rearrangement. A homologous series of 1-(*p*-nitrophenoxy)-ω-anilinoalkane (**1**) gave *N*-(*p*-nitrophenyl)-ω-anilino-1-alkanol (**2**) on irradiation of light (>300 nm). The product **2** was also obtained by the reaction with strong base such as sodium hydride or sodium ethoxide, undoubtedly through nucleophilic attack of the corresponding anilide type anion at the ring carbon atom attached to the ether oxygen, followed by formation of a Meisenheimer type complex. Thus the photorearrangement of **1** to **2** is a photo-Smiles rearrangement.



$O_2N\text{-}C_6H_4\text{-}O(CH_2)_nNHPh \xrightarrow[\text{base}]{h\nu \text{ or}}$

1, $n = 2 - 5$

$O_2N\text{-}C_6H_4\text{-}N(CH_2)_nOH(Ph)$

2

There is only one precedent[3)] for this type of photorearrangement so far as we know. We report here the effects of the chain length in **1** on reaction kinetics and some mechanistic aspects of this photoreaction.

Results and Discussion

Photorearrangement. Solutions of a homologous series of **1** are almost colorless, but become yellow when irradiated with a high-pressure Hg lamp. As an example, the change of the ultraviolet-visible region of the spectrum of *p*-$ON_2C_6H_4O(CH_2)_4NHPh$ (**1**, n=4) in acetonitrile is shown in Fig. 1. The spectral maximum at *ca.* 305 nm, characteristic of *p*-nitrophenoxyl group, disappears with time and a new peak appears at *ca.* 395 nm. This photoreaction was observed in polar solvents such as acetonitrile, alcohols, and tetrahydrofuran, but not in cyclohexane or hexane.

The structure of the products (**2**) was confirmed by spectral and elemental analysis. Their spectral features agreed well with those of the rearranged products obtained by base-induced reaction.[4)] One of the most striking characteristics is the absorption peak at *ca.* 395 nm suggesting the presence of nitroaniline type chromophore. As seen in Fig. 1, the increase of the product (**2**, n=4) can be easily followed with ultraviolet spectroscopy. It also shows isosbestic points, suggesting one-to-one correspondent conversion of **1** to **2**. Since the starting materials showed no appreciable absorption at visible region, the reaction rate was determined simply by the measurement of the time dependence of the intensity at *ca.* 395 nm. Close examination of the Fig. 1 shows that the absorption curves irradiated for a long time deviate slightly from the isosbestic points. This phenomenon is due to the formation of polymeric substances probably produced by the photodecomposition of **2**.

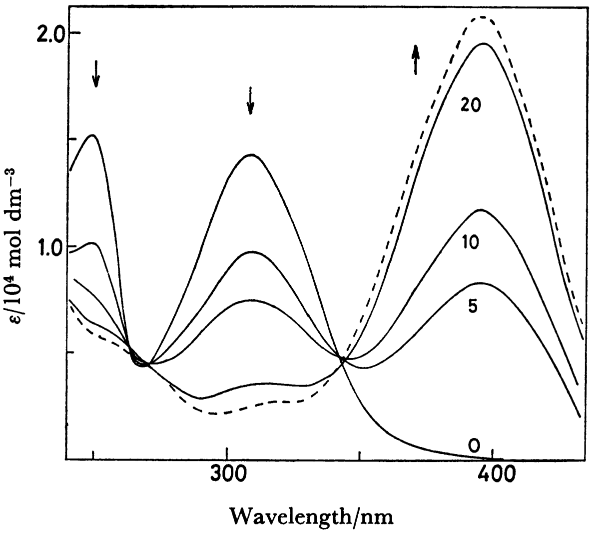


Fig. 1. Absorption spectra of *p*-$O_2NC_6H_4O(CH_2)_4NHPh$ in acetonitrile (0.8×10^{-4} mol/dm^3), irradiated with a high-pressure Hg lamp. Numerals attached to the curves denote time of irradiation in min. The curve in broken line is the absorption spectrum of the product.

In order to avoid the further reaction of **2** which absorbs mainly at longer wavelength region (>330 nm), a filter of an aqueous $NiSO_4$ solution as well as Pyrex was used as the standard conditions for the determination of the rate constants.[5)] Employing acetonitrile as representing aprotic solvent, the photoreaction rates were determined and the relative rate constants (first order reaction) are summarized in Table 1. These are relative values because they are variable with photolysis conditions such as concentration of the solution, intensity of the light, form of the reaction vessel, *etc.*

TABLE 1. RELATIVE INITIAL RATE CONSTANTS (k_{rel}) FOR THE PHOTOREARRANGEMENT OF **1** IN CH_3CN

	$n=2$	3	4	5
k^0_{rel} a)	1.0	2.0	420	120
k^{TEA}_{rel} a,b)	710	400	110	8.6
k^{TEA}_{rel}/k^0_{rel}	710	200	0.25	0.072

a) $k^0_{rel}(n=2)=1.0$. b) Values in the presence of triethylamine (2.84×10^{-2} mol/dm^3).

A notable fact in Table 1 is low reactivity of the lower homologs ($n=2$ and 3) in comparison with the higher ones. It is generally accepted that lower homologs are favored (*i.e.*, react faster or give products in higher yields) in intramolecular reaction. In fact, the Smiles rearrangement of **1** in the presence of sodium hydride in DMF showed the rate order, $n=2\gg3>4>5$.[4] The anomaly in the photoreaction is closely connected with the reaction mechanism and will be discussed in the later part of this paper.

Addition of triethylamine or pyridine to the solution accelerated the reaction remarkably. The amines are weak bases unable to catalyze the rearrangement of **1** in the dark. The results for triethylamine are summarized in Table 1. The resulting reactivity order with regard to n is the same as that observed in the base-catalyzed reaction. In the third row of Table 1, the ratios of the rate constants in the presence *vs.* in the absence of the amine are shown. The rate increase in the lower homologs is in the order of 10^2, but the higher homologs showed a slight decrease. This rather unexpected behavior of the higher homologs is a result of a concomitant photoreaction of **1** with the added amine. The electronic spectrum of the solution containing triethylamine showed a new peak at *ca.* 290 nm in addition to those of **2** on irradiation. This side reaction, which apparently retarded the rate, was also observed in the lower homologs but to a far less extent. Since irradiation under the same conditions of an acetonitrile solution of *p*-nitrophenetole containing the amine induced a similar spectroscopic behavior, the side reaction observed in **1** is probably due to a reaction between *p*-nitrophenoxyl moiety and triethylamine whose photoreductive capability is well known.[6]

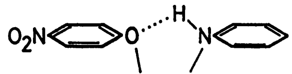
In order to see the effect of protic solvent, the rate constants in methanol were determined and summarized in Table 2.

TABLE 2. RELATIVE INITIAL RATE CONSTANTS (k_{rel}) FOR THE PHOTOREARRANGEMENT OF **1** IN CH_3OH

	$n=2$	3	4
k_{rel} a)	1.0	0.5	1.0
k^{TEA}_{rel} a,b)	75	30	4.0
k^{TEA}_{rel}/k_{rel}	75	60	4.0

a) $k_{rel}(n=2)=1.0$. b) Values in the presence of triethylamine (2.84×10^{-2} mol/dm^3).

It is interesting that there is little difference in the rate of three homologs studied, though considering the distance of the two reacting centers, the rate of $n=4$ should be regarded still as unusually large. Comparison of the absolute values of k^0 in methanol with those in acetonitrile shows acceleration by a factor of 10 and 2 in methanol for $n=2$ and 3, respectively, and reduction by 0.02 for $n=4$. The observed rate acceleration may be due to the destruction of intramolecular N–H···O hydrogen bond which is present in these lower homologs[7] and arranges the molecule in conformation with two π-electron systems far apart, unfavorable situation for exciplex formation (**3**). Different solvating manner of methanol from acetonitrile for **1** in the ground and excited states and for reaction intermediates is also an important factor, though the details are yet unknown.



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In the presence of triethylamine, the absolute k^{TEA}'s of the $n=2$ homolog in these two solvents are nearly the same, implying the upper limit of the reaction rate of this homolog. The smaller accelerating effect of the base in $n=3$ (one order less than in acetonitrile) may be due to lower activity of triethylamine in this protic solvent. It is notable that a small but definite rate acceleration by the amine is observed for the $n=4$ homolog. In contrast to the reaction in acetonitrile, no reaction of **1** with the amine was observed in methanol.

Some Mechanistic Aspects. The effect of the amine suggests ionic character of the photoreaction. The most probable ionic process is abstraction of the N–H proton by the amine, thus producing an anilide type anion, $p\text{-}O_2NC_6H_4O(CH_2)_n\overset{\ominus}{N}Ph$, which then takes the same course as in the Smiles rearrangement. The same reactivity order with regard to n in both cases supports this possibility. The key step in this mechanism is the increase of the acidity of the N–H group on absorption of ultraviolet light. There are two possibilities: (i) The acidity of the anilino moiety increases on excitation[1] as is the case in naphthylamine[8] and phenols;[9] (ii) Intramolecular exciplex or excited state of intramolecular charge-transfer interaction may facilitate proton release from the N–H group. Of these, the mechanism (ii) has been proved to be valid by Yokoyama *et al.*[10] They confirmed the presence of a radical ion pair (**4**)

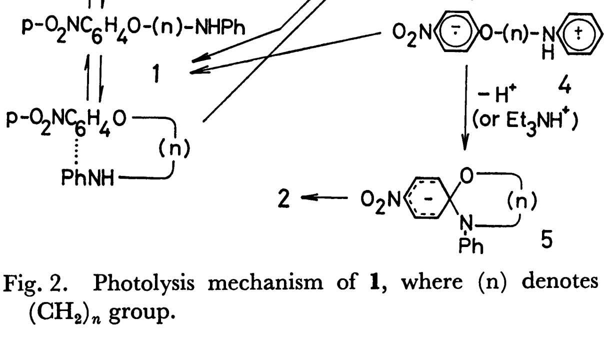

Fig. 2. Photolysis mechanism of **1**, where (n) denotes $(CH_2)_n$ group.

and a spiro type Meisenheimer complex (**5**) by means of time dependent transient absorption spectral measurement of solutions irradiated with N_2-laser pulse. Therefore a probable photorearrangement mechanism is as depicted in Fig. 2.

One of the possible processes which lead to the ion pair may start with the excitation of the *p*-nitrophenoxyl chromophore absorbing at *ca.* 305 nm, followed by formation of an intramolecular exciplex. Another one leading to a similar exciplex may be the excitation of the molecule in the state of intramolecular charge-transfer interaction.[11] Since the charge-transfer interaction in the ground state is very weak, the ionic character of the exciplex is large and the electron transfer to form the radical ion-pair (**4**) is probably a smooth process. In the step following the exciplex formation, an electron from the anilino group in **1** is transferred to the nitrophenoxyl group, and the resulting radical cation moiety has an N–H group with sufficiently strong acidity to release its proton. Here, the role of triethylamine is evident, because the basicity of the amine is far stronger than acetonitrile. The failure of the photo-Smiles rearrangement in cyclohexane or hexane is also apparent, as these solvents are poor acceptors of proton and have meager solvating power for ions. In fact, the formation of the ion pair (**4**) has not been detected in these solvents.[10]

There remains a question why the reactivity of the lower homologs in acetonitrile is abnormally low in the absence of bases. The anomaly is in the lower homologs ($n=2$ and 3), and not in the higher ones ($n=4$ and 5). Since the process subsequent to the release of the N–H proton should be the same as the Smiles rearrangement, the step where the reaction rates in question are mainly determined is after the excitation of **1** and before the proton release. Therefore, the factors governing the reactivity may be concerned with the fate of excited chromophores and/or of the radical ion pair.

It should be mentioned here that the lifetimes of the ion pair, **4**, for $n=2$, 3, and 4 are 65, 73, and 98 ns, respectively.[10] Similar effect of chain length on the process of intramolecular fluorescence quenching has been reported.[12] Since the electron return process and conformational change to form a sandwich type form is far faster than proton transfer,[13] the reason of the low reactivity in the absence of the amine is probably due to the presence of effective quenching routes for the ion pairs of the homologs with short chain length.

Experimental

Reaction Kinetics of Photolysis. A 200-cm³ solution was irradiated with a 100 W high-pressure Hg lamp equipped with a Pyrex cooling jacket, through which a solution of nickel sulfate (500 g $NiSO_4$/dm³ aqueous solution) was passed. The lamp was immersed in a vessel containing the solution of $0.8—0.9\times10^{-4}$ mol/dm³. For the determination of the reaction rate, the solution was circulated through a flow-cell set in a Hitachi 100-50 spectrophotometer. Time dependence of the increase of the characteristic absorbance of the product at *ca.* 395 nm was recorded and the initial rate constant calculated, assuming first-order reaction.

Solvents. Acetonitrile (Wako, G. R. grade) was distilled from the mixture with phosphorus pentaoxide (5 g/dm³ CH_3CN). Methanol (Wako, G. R. grade) was used after distillation.

Preparation of ***2***. *General Procedure*: A 250-cm³ acetonitrile solution containing *ca.* 50 mg of **1**[10] is irradiated with a 100 W high-pressure Hg lamp through Pyrex and aqueous $NiSO_4$ filters. For the solutions of $n=2$ and 3 homologs of **1**, 2 cm³ of triethylamine was added. After removing the solvent, the residue was dissolved in dichloromethane, and the solution was passed through a column packed with silica gel using benzene–dichloromethane (1 : 1) and dichloromethane as eluents.

N-*(*p*-Nitrophenyl)-2-anilinoethanol (**2**, $n=2$)*: This compound was obtained in 87% isolated yield as dark red liquid; 3,5-dinitrobenzoate, mp 172—173 °C; UV_{max} (95% EtOH), 392 nm (ε 19200); NMR ($CDCl_3$) $\delta=2.72$ (1H s, OH), 3.8 (4H, m, CH_2CH_2), 6.57 and 7.82 (4H, two d, $J=9$ Hz, *p*-$O_2NC_6H_4$), and 7.2 (5H, m, C_6H_5); MS (70 eV), *m/e* 258 (M^+), 227 ($O_2NC_6H_4(Ph)NCH_2^+$), and 181 (227−NO_2).

Found: C, 64.97; H, 5.43; N, 10.68%. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.10; H, 5.46; N, 10.85%.

N-*(*p*-Nitrophenyl)-3-anilino-1-propanol (**2**, $n=3$)*: This compound was obtained in 74% isolated yield as red liquid, 3,5-dinitrobenzoate, mp 124—125 °C; UV_{max} (95% EtOH), 391 nm (ε 18900); NMR ($CDCl_3$)$\delta=1.94$ (2H, m, C–CH_2–C), 2.91 (1H, s, OH), 3.71 and 3.88 (4H, two t, NCH_2 and OCH_2), 6.57 and 7.87 (4H, two d, $J=9$ Hz, *p*-$O_2NC_6H_4$), and 7.2 (5H, m, C_6H_5); MS (70 eV), *m/e*, 272 (M^+), 227, and 181.

Found: C, 66.27; H, 5.84; N, 10.37%. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.15; H, 5.92; N, 10.29%.

N-*(*p*-Nitrophenyl)-4-anilino-1-butanol (**2**, $n=4$)*: This compound was obtained in 82% isolated yield as yellow needles: mp 75—76 °C; UV_{max} (95% EtOH), 391 nm (ε 19400); NMR ($CDCl_3$) $\delta=1.7$ (5H, m, C–CH_2–CH_2–C and OH), 3.7 (4H, m, NCH_2 and OCH_2), 6.50 and 7.87 (4H, two d, $J=9$ Hz, *p*-$O_2NC_6H_4$), and 7.2 (5H, m, C_6H_5); MS (70 eV), *m/e*, 286 (M^+), 227, and 181.

Found: C, 67.27; H, 6.43; N, 9.59%. Calcd for $C_{16}H_{18}N_2O_3$: C, 67.11; H, 6.34; N, 9.78%.

N-*(p-Nitrophenyl)-5-anilino-1-pentanol (**2**, $n=5$)*: This compound was obtained in 61% isolated yield as dark red liquid; UV_{max} (95% EtOH), 389 nm (ε 19400); NMR ($CDCl_3$) $\delta=$ 1.55 (7H, m, C–CH_2–CH_2–CH_2–C and OH), 3.8 (4H, m, NCH_2 and OCH_2), 6.79 and 8.28 (4H, two d, $J=10$ Hz, *p*-$O_2NC_6H_4$), and 7.5 (5H, m, C_6H_5); MS (70 eV), *m/e*, 300 (M^+), 227, and 181.

Found: C, 67.74; H, 6.93; N, 9.42%. Calcd for $C_{17}H_{20}N_2O_3$: C, 67.98; H, 6.71; N, 9.33%.

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