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SELECTIVE PHOTOTRANSFORMATION OF HYDROXY-SUBSTITUTED AROMATIC NITRONES INTO *N*,*N*-DIARYLFORMAMIDE DERIVATIVES SHOWING A NOVEL CONFORMATIONAL ISOMERISM

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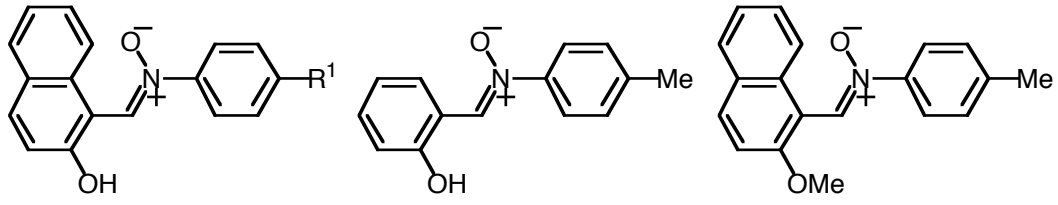
Abstract– On irradiation in acetonitrile at 366 nm, photorearrangements of the title aromatic nitrones (**1**) proceeded to give selectively *N*,*N*-diarylformamides, which showed a novel conformational isomerism without undergoing large substituent, solvent, and temperature effects. An analysis of substituent and solvent effects on the product distribution confirmed that a hydrogen-bonding interaction with the ring nitrogen in oxaziridine intermediates plays a crucial role in inducing the selective transformation of **1** into the corresponding formamide derivatives.

Excited-state chemistry has continued to contribute to the development of a variety of functional molecules. In recent years much attention has been directed to studies regarding the photochemical control of refractive index of polymer film, owing to its potential application to graded-index-type polymer optical fiber.[1a–f] Miyata and Ritter groups reported that the photoisomerization of substituted aromatic nitrones into the corresponding oxaziridine derivatives effectively contributes to lowering the refractive index of polymer films.[1d,f] While the excited-state reactivities of these nitrone derivatives have been extensively explored from both synthetic and mechanistic points of view,[2] their findings allow us to emphasize that photochemistry of aromatic nitrones is of great practical value. In a previous study it was shown that the photoisomerization of 1-naphthyl-substituted nitrone derivative procceds quantitatively to give the corresponding oxaziridine, the photoreactivity of which is strongly dependent on the properties of solvent and sensitizer used.[3] It is, thus, of significance to scrutinize substituent and solvent effects on the photoreactivity and photoproduct distribution of aromatic nitrone derivatives. Taking into account that the introduction of a hydroxy group into aromatic nitrones enables the formation of intramolecular hydrogen bonding and exerts great effects on both their excited-state reactivity and the ring-opening process of nitrone-derived photoproducts, possibly

oxaziridines, we designed and synthesized *N*-(2-hydroxy-substituted arylmethylene)arylamine *N*-oxides (**1a–c**) and related aromatic nitrone derivative (**1d**), hoping to shed much light on the photochemical behavior of these nitrone derivatives.[4]



1a (R^1 = Me)
1b (R^1 = H)

1c

1d

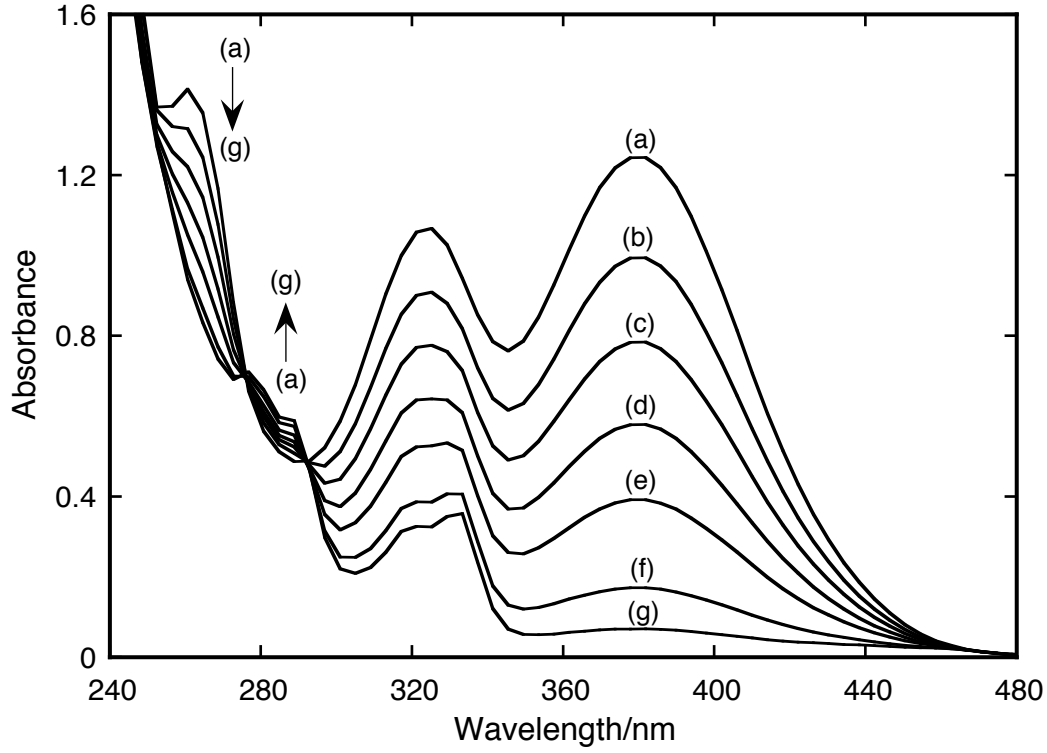


Figure 1. Absorption spectral changes of **1a** (1.0×10^{-4} mol dm^{-3}) during irradiation. Irradiation time/min: (a) 0; (b) 10; (c) 20; (d) 30; (e) 40; (f) 60; (g) 80.

In Figure 1 are typically shown UV absorption spectral changes caused by the 366 nm irradiation of a nitrogen-saturated acetonitrile solution of **1a** at room temperature. When the photoreaction went to completion, the strong UV absorption of the starting **1a** at 379 nm virtually disappeared with appearance of the 330 nm absorption, while there were two isosbestic points at 275 and 293 nm. In order to isolate the product and determine its structure, a nitrogen-saturated acetonitrile solution of **1a** (100 mL, 4.0×10^{-3} mol dm^{-3}) was irradiated with light of wavelengths longer than 340 nm (from a 450 W high-pressure Hg lamp) for 90 min at room temperature (conversion 45%, UV spectral analysis). The reaction mixture containing only **1a** and the single product (HPLC analysis) was subjected to thin layer chromatography over silica gel (eluent: ethyl acetate-hexane), which allowed us to isolate the product in a pure form. Because the isolated

product existed as two conformers in solution (^{1}H NMR spectral analysis), it was very difficult to unambiguously determine its structure. The successful growth of single crystal made it possible to establish that the photorearrangement of **1a** proceeds to afford selectively *N*-(2-hydroxynaphthyl)-*N*-(4-tolyl)formamide (**2a**, 40% isolated yield), as shown in Figure 2.[5,6]

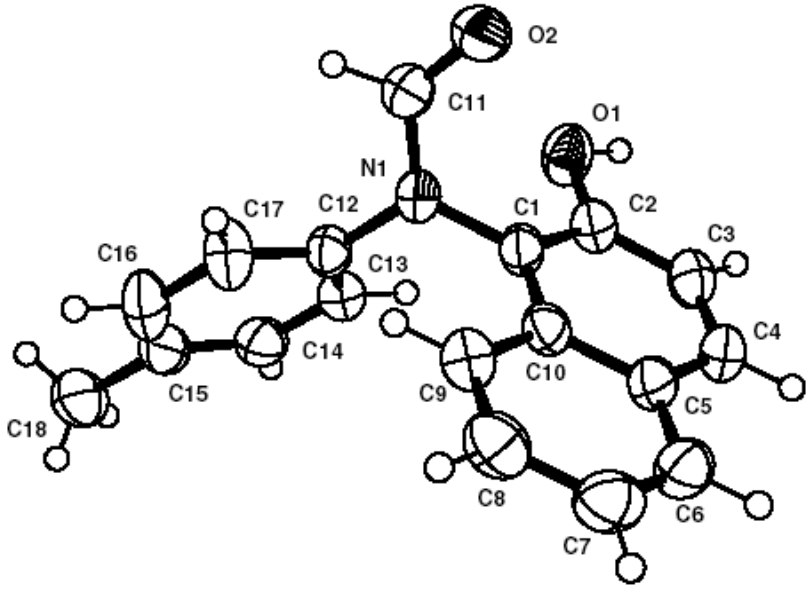


Figure 2. ORTEP drawing of **2a**.

One conformer of the formamide derivative (**2a**) exhibited its formyl and hydroxyl proton signals at 8.86 and 6.24 ppm in chloroform-*d*, respectively (conformer A) and the other conformer at 8.27 and 6.34 ppm, respectively (conformer B). The area ratio of the former proton signal to the latter was 1.7 to 1.0 at 24 ℃. In order to estimate the structure of these two conformers, energy-minimized conformers (MM2) and heats of formation (ΔH_f, PM5) were calculated.[7] As shown in Figure 3, there were two energy-minimized conformers: One conformer is very similar to that given in Figure 2, where the formyl and hydroxy groups are situated in the same side (ΔH_f = –80.74 kJ mol^{-1}), and in the other conformer these two groups are located in the opposite side (ΔH_f = –79.66 kJ mol^{-1}). A comparison of the ΔH_f values allows us to predict that the former conformer would be somewhat more stable than the latter and, hence, would give its formyl and hydroxyl proton signals at 8.86 and 6.24 ppm, respectively.

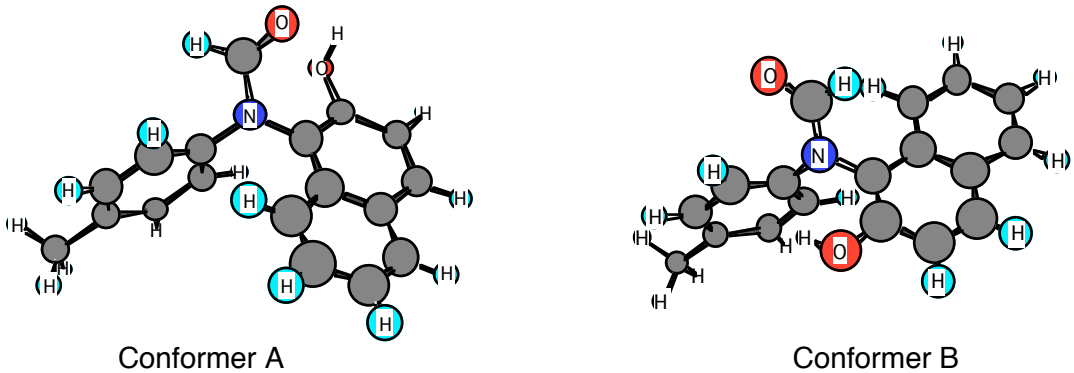
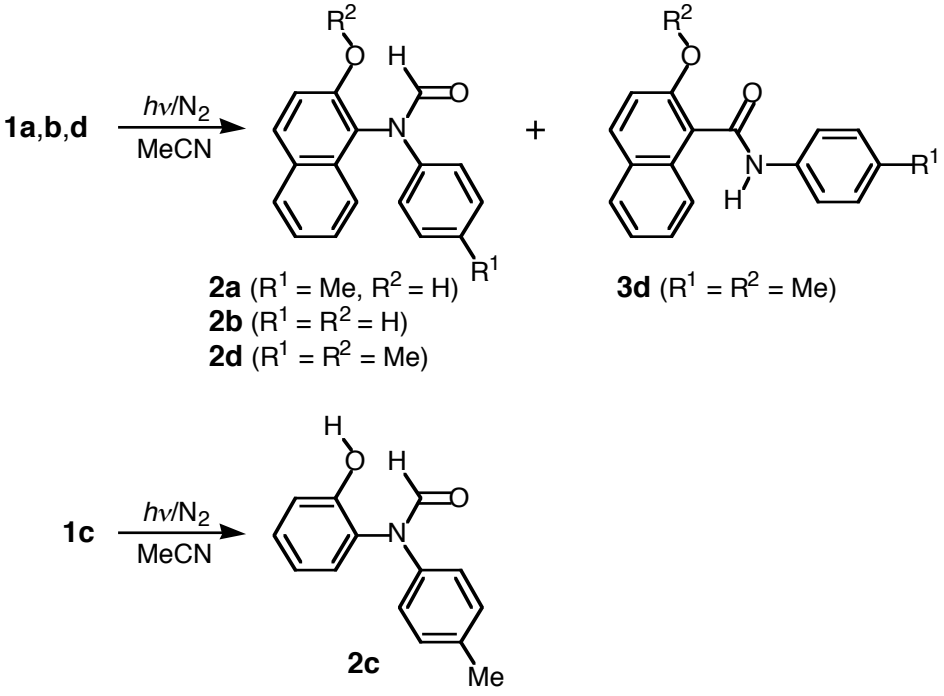


Figure 3. Energy-minimized conformers A and B of **2a**.

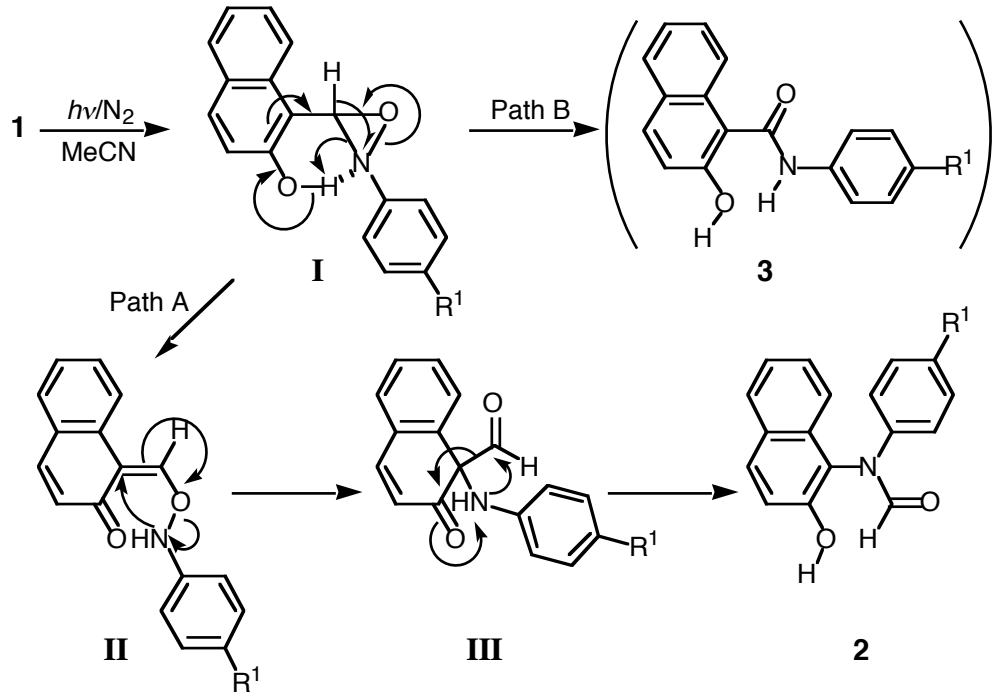
An analysis of the product distribution derived from the reactions of **1b** and **1c** (4.0×10^{-3} mol dm^{-3}) in nitrogen-saturated acetonitrile under the same irradiation conditions revealed that **1b** and **1c** quantitatively form the corresponding rearrangement products (**2b** and **2c**) whereas 1-naphthanilide derivative (**3d**) is obtained along with the rearranged product (**2d**) in a 5:4 mole ratio (^{1}H NMR spectral analysis, Scheme 1). Interestingly, the novel conformational isomerism described above was observed also for the other *N*,*N*-diarylformamide derivatives (**2b**–**d**). The proportions of the conformer A to the conformer B were estimated to be 1.5 to 1.0 (**2b**), 2.3 to 1.0 (**2c**), and 1.3 to 1.0 (**2d**) in chloroform-*d* at 24 °C, confirming that the conformer ratio is not very sensitive to structural changes. In addition, this ratio for **2a** was slightly increased in dimethyl sulfoxide-d_6 (1.7/1.0→2.0/1.0) while an increase in temperature shifted the conformational equilibrium in dimethyl sulfoxide-d_6 to some extent (2.0/1.0 at 24 °C→1.7/1.0 at 80 °C). These findings demonstrate, therefore, that substituent, solvent, and temperature exert only small effects on the observed equilibrium.



Scheme 1

In order to compare the excited-state reactivities, quantum yields (Φ_{-1}) for the disappearance of **1a**–**d** (1.0×10^{-4} mol dm^{-3}) were determined in acetonitrile at room temperature [Φ_{-1} = 0.039±0.002 (**1a**), 0.036±0.002 (**1b**), 0.045±0.002 (**1c**), and 0.59±0.03 (**1d**)].[8] An intramolecular hydrogen bond (that must be formed between the hydroxyl hydrogen and the *N*-oxide oxygen in **1a**) lowers the quantum yield by an order of magnitude, thus demonstrating that the hydrogen-bonding interaction greatly accelerates the deactivation of excited-state **1** to result in a decrease in the reactivity of the *N*-oxide oxygen toward the iminomethyl carbon. This result is consistent with the occurrence of photoisomerization of **1** to the corresponding oxadiridine intermediate (**I**) at the first step of the observed rearrangement reaction, as shown in Scheme 2. The previous finding that 3-(1-naphthyl)-2-(1-naphthylmethyl)oxaziridine is stable in

acetonitrile and can be isolated in a good yield allows us to propose that 2,3-diaryloxadirizines are highly reactive and, hence, readily undergo hydrogen bond-assisted C–N bond cleavage to give the hydroxylamine intermediate (**II**, Path A in Scheme 2).[3] The Smiles-type rearrangement of **II** may eventually afford *N*,*N*-diarylformamide derivatives (**2**) *via* the intermediate (**III**). As already described above, replacement of the hydroxy group in **1a** by the methoxy group produces **2d** and **3d** in comparable yields. The lack of intramolecular hydrogen bond in the **1d**-derived oxaziridine (**I**) is considered to enhance the relative rate for the N–O bond cleavage and the subsequent 1,2-hydrogen shift in this oxaziridine intermediate, which take place in competition with the C–N bond fission (Path B in Scheme 2). In addition, the formation of **2d** suggests that the presence of electron-donating substituents such as hydroxy and methoxy groups plays a role in bringing about the C–N bond cleavage in a high efficiency.



Scheme 2

Recently, it was found that trifluoroacetic acid is an effective catalyst in causing the oxidative rearrangement of *C*-aryl- or alkyl-*N*-arylaldimines to *N*,*N*-disubstituted formamides, which is assumed to proceed through an oxaziridine intermediate.[9] This finding suggests an important role of hydrogen-bonding interaction between the acid and, presumably, oxaziridines, as already described above. If so, it is expected that the irradiation of **1d** in the protic polar solvent, methanol, would give **2d** in preference to **3d**. Interestingly, on irradiation of **1d** (4.0×10^{-3} mol dm^{-3}) in methanol at 366 nm, the exclusive formation of **2d** was observed (^{1}H NMR spectral analysis). Therefore, we were led to conclude that the formation of a hydrogen bond with the oxaziridine-ring nitrogen plays an essential role in inducing the selective C–N bond cleavage in this ring that enables the quantitative transformation into *N*,*N*-diarylformamides (**2**).

A few synthetic routes to *N*,*N*-disubstituted formamide derivatives are known but their yields are not so high and strongly dependent on steric and electronic factors of substituents introduced.[9,10] Additionally, there is no synthetic method (of these derivatives) which employs photochemical rearrangements of hydroxy-

substituted aromatic nitrones, the rearranged products of which exhibit a novel conformational isomerism in solution. By using methanol as a solvent we may synthesize selectively various kinds of formamide derivatives, and also the presence of a hydroxy group in the rearranged products makes the derivatization of these products possible.

ACKNOWLEDGMENTS

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4. Selected data for **1a**: mp 149.0–149.5 °C (ethanol); IR (KBr): ν/cm^{-1}= 3420, 3064, 1623, 1572; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 2.45 (3H, s), 7.21 (1H, d, *J*= 8.6 Hz), 7.33 (2H, d, *J*= 6.8 Hz), 7.40 (1H, dd, *J*= 7.0, 7.3 Hz), 7.54 (1H, dd, *J*= 7.0, 8.5 Hz), 7.75 (2H, d, *J*= 6.8 Hz), 7.76 (1H, d, *J*= 8.6 Hz), 7.81 (1H, d, *J*= 7.3 Hz), 7.92 (1H, d, *J*= 8.5 Hz), 8.85 (1H, s), 12.54 (1H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ= 21.2, 108.9, 121.0, 121.7 (2C), 122.4, 123.9, 127.9, 128.2, 129.1, 129.9 (2C), 133.0, 135.5, 138.5, 140.8, 143.9, 162.1. Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 78.26; H, 5.46; N, 5.43. Spectroscopic and physical properties of **1b–d** will be given elsewhere.
5. Selected data for **2a**: mp 177.0–177.5 °C (ethyl acetate-hexane); IR (KBr): ν/cm^{-1}= 3199, 2895, 1658, 1581; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 2.26 (1.11H, s), 2.28 (1.89H, s), 6.24 (0.63H, s), 6.34 (0.37H, s), 6.99–7.08 (4H, m), 7.09 (0.63H, d, *J*= 8.6 Hz), 7.18 (0.37H, d, *J*= 8.6 Hz), 7.25-7.33 (0.74H, m), 7.31–7.37 (1.26H, m), 7.44 (0.37H, dd, *J*= 7.4, 8.1 Hz), 7.49 (0.63H, dd, *J*= 6.9, 8.0 Hz), 7.58 (0.37H, d, *J*= 8.6 Hz), 7.66 (0.63H, d, *J*= 8.6 Hz), 7.75 (0.63H, d, *J*= 8.0 Hz), 7.78 (0.37H, d, *J*= 8.1 Hz), 8.27 (0.37H, s), 8.86 (0.63H, s); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ= 20.8, 22.6, 118.0, 118.6, 119.14, 119.14, 121.1, 121.4, 121.94, 121.94, 122.98, 122.98, 123.6, 123.9, 127.3, 127.9, 128.25, 128.30, 129.1, 129.4, 129.53, 129.53, 130.09, 130.09, 130.4, 130.8, 131.0, 132.4, 135.7, 136.2, 137.0, 138.6, 150.9, 152.2, 163.7, 164.5. Anal. Calcd for $C_{18}H_{15}NO_2$: C, 77.96; H, 5.45; N, 5.05. Found: C, 77.77; H, 5.48; N, 5.09. Spectroscopic data for **2b–d** and **3d** were consistent with their

structures and will be given elsewhere.

6. Crystal data for **2a**: $C_{18}H_{15}NO_2$, f_w= 277.31; colorless prism, 0.45×0.43×0.38 mm, monoclinic, space group $P2_1/c$; a= 10.876(5), b= 9.390(4), c= 14.517(7) Å, β= 104.83(4)°, V= 1433.2(11) Å^3; Z= 4; D_{calcd}= 1.285 g cm^{-3}; R= 0.0523, $wR(F^2)$= 0.1653.
7. MM2 and PM5 calculations were accomplished by using CAChe 5.0 for Windows available from Fujitsu Ltd (2002).
8. Quantum yields were determined at low conversions (10–15%) of the starting **1** according to the method of Hatchard and Parker which employs a potassium trioxalatoferrate(III) actinometer (C. G. Hatchard and C. A. Parker, *Proc. R. Soc. London, Ser. A*, 1956, **235**, 518). All the quantum yields are an average of more than five determinations.
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