Novel Oxazabicycles as a New Class of Photochromic Colorants

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ABSTRACT

A new photochromic colorant with an oxazabicyclic moiety has been synthesized by an efficient method. It turns pale red upon UV irradiation and undergoes reverse reaction while being heated. This work may open an exciting new avenue for future development of the photochromic dyes with novel molecular structures.

Owing to their practical applications in ophthalmic lenses, organic photochromic dyes have long attracted great attention. Extensive investigations have been carried out on bisdiarylethenes, bispyrans, bisbenzodihydropyrenes, andbishydroindolizines. While modifications of the existing photochromes may still generate compounds with unprecedented properties, new classes of organic photochromic dyes with novel molecular structures should be developed for use as suitable materials for optical memory media, photooptical switch components, and other applications.

In our continuing efforts to develop new therapeutic agents for anti-coagulation therapy in humans by inhibiting the activity of vitamin K 2,3-epoxide reductase (VKOR), we recently discovered a conformationally restricted VKOR inhibitor with a coumarin-containing dioxobicyclic and oxazabicyclic skeleton. Upon ultraviolet irradiation of oxazabicyclic colorant 1 (see Scheme 1), a mixture of quinoline-containing derivatives 2 and 3 as well as 4-hydroxycoumarin were detected. This result suggested that the photoreaction of 1 should involve a C–O bond cleavage at the junction of the two heterocycles, along with a subsequent aromatization.

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We thus speculate that this skeleton may have the potential to function as a new class of photochromic systems if the subsequent aromatization process can be prohibited. As for a strategic design, incorporation of two alkyl groups (i.e., dimethyl groups) at the C(9)-position of this oxazabicyclic skeleton may prevent the undesired aromatization reaction upon UV irradiation. Herein, we report the efficient synthesis of novel oxazabicycles 7a–e, in which 7c is demonstrated to represent a new class of photochromic colorant.

Scheme 2 shows the preparation of gem-dimethyl-substituted oxazabicycles 7a–e. It began with a MgSO₄-mediated condensation of p-anisidine and substituted benzaldehydes 4a–e to afford the imines 5a–e, followed by a Yb(OTf)₃-catalyzed coupling with isobutyraldehyde to give the cyclized alcohols 6a–e. The reaction of 6a–e with 4-hydroxycoumarin in the presence of a catalytic amount of p-toluene-sulfonic acid under reflux conditions yielded the target compounds 7a–e (see Supporting Information for detailed characterization). The aforementioned three reaction steps could all be acid-catalyzed, and the bond formation during the construction of the bicyclic skeleton was highly efficient.

Among the prepared compounds, the oxazabicycle 7c, which contained a nitro substituent at the ortho position of the bridgehead benzene ring, exhibited salient photochromic behavior. Upon ultraviolet irradiation (320 nm), the oxazabicycle 7c in CH₃CN turned from colorless to pale red, as shown in the graphic abstract. Spectroscopically, with the increase of exposure time, a new absorption band with the peak wavelength around 500 nm gradually increased. Although an isosbestic point was lacking during photolysis, the absorbance at 500 nm showed a smooth, continuous growth and reached a plateau (see inset of Figure 1), implying the stationary conversion to the 500 nm absorbing species.

Isolation of the photogenerated product proved to be difficult since it reverted easily back to the original form under weakly acidic conditions on the silica gel column. Alternatively, upon methylation of the photogenerated product with diazomethane, the resulting methylated derivative 8 was stable enough to be isolated for further characterization (Scheme 3). The X-ray crystal structure of 8 (see Figure S1 in the Supporting Information) clearly presents the similarities to 7c in its mainframe, except for the cleavage of the O(8)–C(1) bond (see Scheme 1 for the numerical sequence, which is renamed to the O(3)–C(17) bond in Figure S1) in the oxazabicyclic moiety and the methylation at the O(8) site (see Scheme 3). The results lead us to conclude that 7c may simply undergo the O(8)–C(1) bond

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temperatures (Figure 2b). Taking monitoring time. The first-order decay dynamics are sup-

tion and hence a large reduction of the entropy factor. It is

photolysis period, the same residual absorbance was observed upon performing the 7z → 7c process in various temperatures ranging from 20 to 60 °C. We thus discarded the possibility of thermal equilibrium between 7c and 7z, concluding instead the generation of side products. This viewpoint is also supported by a theoretical approach, in which 7c is more stable than 7z (zwitterionic form) by >30 kcal/mol (vide infra). The temperature-independent side product formation during the reverse 7z → 7c reaction also eliminates the possibility of its origin being thermal decomposition of 7z. Instead, the side product was produced during the photoinduced 7c → 7z process. In addition to the major 7z formation, it is plausible that, similar to the ultraviolet irradiation of oxazabicycle 1, the photoreaction of 7c, at a small percentage, involves a C–O bond cleavage at the junction of the two heterocycles, along with a subsequent aromatization. Being solely dependent on the change of 500 nm absorbance from 7z, the first four (1) → (2) → (1) (see Scheme 3) cycles are depicted in the inset of Figure 2a. After the fourth cycle, the 7z production decreases to ~50% of its first photoconversion.

Figure 2. (a) Thermal bleaching of 7z (in CH3CN) around 500 nm at 60 °C from 0 to 36 min with increments of 2 min. Inset: Absorbance at 500 nm in the first four cycles, in which each cycle consists of 3 h UV irradiation and 90 min thermal bleaching at 60 °C. (b) The plot of ln A500nm versus decay time at various temperatures. Inset: The plot of ln krev versus 1/T.

To gain further insight into the reaction thermodynamics, we carried out a molecular simulation utilizing the density function theory (DFT) method. Under the full geometry optimization (B3LYP/6-31G*), 7c was calculated to be lower in energy than 7z by 34.83 kcal/mol. Applying the TDMPW1K method, the S0 → S1 transitions were calculated to be 28 090 (356 nm) and 13 158 cm−1 (760 nm) for 7c and 7z, respectively, the results of which, especially for 7z, are significantly lower in energy than the respective peak wavelength at ~310 and ~500 nm extracted from the absorption spectroscopy. For further improvement, using IEFPCM model (see Supporting Information) to consider the solvent effect of acetonitrile, the S0 → S1 transition of 7z is shifted from 13 158 to 18 762 cm−1 (533 nm), while it
remains nearly unchanged for 7c (350 nm). The large solvation change in 7z further implies its zwitterionic property. According to the calculation, the electronic excitations between S₀ and S₁ of 7c is dominated by the HOMO → LUMO excitation (Figure 3), in which the electron density of HOMO is mainly located on the lone pair of O(8) atoms and the p-methoxybenzamine moiety. Conversely, the electron density is transferred to the NO₂ group in the LUMO. The net change of the electron density during the HOMO → LUMO transition is expected to cause the C=O bond weakening and consequently cleavage. We also performed a similar calculation on 7t, considered to be another possible neutral product (see Scheme 3). The calculated S₀→S₁ transition of 28570 cm⁻¹ (350 nm) is much higher in energy than that of the product (7z) absorption peak experimentally resolved to be 500 nm. The result justifies the assignment of 7z to a zwitterionic species. Theoretically, the 7c → 7z formation involves only the cleavage of C(sp³)―O bonding at the junction of the heterobicycle, while for 7t, if it were the product, in addition to the bond cleavage, another hydrogen transfer from the amino group (N(2)) on O to be necessary, leading to a dynamically unfavorable pathway.

Among 7a–e only 7c exhibits the aforementioned photochromic properties. The fact that only the oxazabicycle with a nitro substituent at the ortho position of the bridgehead benzene ring exhibited the expected photochromic behavior implied that the ortho substituent, but not meta and para, on the bridgehead benzene ring plays an important role in the photochemistry. We initially speculated that the increasing steric hindrance between the ortho substituent and the nearby methyl groups on the heterobicyclic skeleton made 7c more susceptible to a C=O bond rupture than the corresponding p-nitro-substituted 7b. However, neither the o-chloro-functionalized (7d) nor the o-methoxy-substituted (7e) analogue exhibits any photochromic behavior, suggesting that factors other than the steric effect govern the photochromism. An additional experiment was also performed and found no photochromic property when the amino group (N(2)) on 7c was methylated. The result thus drew our attention on the possible role of hydrogen bonding formation between the iminium hydrogen (N(2)―H) and nitrooxygen (N(10)―O). The result of molecular simulation for 7c produced an estimated distance between the oxygen atom on the o-nitro group and the amino hydrogen atom of 2.39 Å (see Figure S2 in the Supporting Information), while this distance for 7z even decreases to as short as 1.98 Å. It is thus reasonable to propose that 7z can be further stabilized via enhancing the intramolecular hydrogen bonding strength between the iminium hydrogen and the nitrooxygen. This hypothesis is supported by the result that 7z is calculated to be 34.2 kcal/mol (adding CH₃CN as the solvent) higher in energy than 7c, while based on a similar method, we calculated the energy of zwitterionic product of 7b, if there were any, to be higher in energy than 7b by 39.3 kcal/mol. In comparison, the difference of ~5 kcal/mol manifests the stabilization energy given by the hydrogen bonding formation in 7z. We thus tentatively propose that the strong N(2)―H―O―N(10) intramolecular hydrogen bonding plays a certain role in “trapping” the 7z species. Note that similar hydrogen bonding formation is not evident in other synthesized analogues presented in this study.

We have also made attempts to analyze the product yield in a more quantitative manner. Using a 30 mW/cm² 355 nm Nd:YAG pulse laser to illuminate the entire volume of 3 mL of 7c solution (7.8 × 10⁻⁵ M in acetonitrile) for 100 min, we then observed that the absorbance at 500 nm was increased from 0.003 to 0.172, corresponding to an increase of 4.9 × 10⁻³ M of the 7z production. Taking the ratio of the number of 7z molecules being produced versus the number of photons being absorbed, the yield of 7z production was then estimated to be 0.12 ± 0.02%.

Since the above photochromic phenomena, the associated dynamics, and efficiency are independent of O₂, the reaction less likely takes place in the triplet manifold. To draw the relative thermodynamics in the excited singlet state, we simply added the observed S₀→S₁ absorption peak in terms of energy to the calculated energy for 7c and 7z. The result, depicted in Scheme 4 of the Supporting Information, indicates that 7c → 7z is thermodynamically favorable only by ~1.0 kcal/mol along the S₁ state. Alternatively, it is more plausible that the photochromism proceeds via a nonadiabatic (i.e., surface crossing) process from S₁ (7c) to S₀ (7z). Nevertheless, at this stage, whether the reaction takes place strictly in the excited state or via crossing to the ground state potential energy surface is pending detailed dynamics approaches.

The oxazabicycle 7c reported here, to the best of our knowledge, represents the first example of a heterobicyclic molecule exhibiting satisfactory photochromic properties. Although the overall photochromism cycle is relatively slow and the maximum absorption at 500 nm (ε ~500 M⁻¹ cm⁻¹, see Figure 1) is low, we believe that 7c or its analogues may still merit future applications. For example, the 7z → 7c reverse reaction is of importance in that the ~34 kcal/mol is chemically stored in 7z and may be re-exploited in the presence of suitable catalysts. Moreover, in the current system, both 7c and 7z are nonluminescent despite their anchoring coumarin moiety. Thus, work focusing on the improvement of the reaction reversibility as well as the utilization of fluorescence based on coumarin analogues to enhance the detection should be of great interest. We thus believe that this work may open an exciting new avenue for future development of the photochromic dyes with novel molecular structures.

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Supporting Information Available: Additional experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.