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PHOTOCHEMICAL OXYGENATION OF OLEFINS BY HETEROCYCLIC N-OXIDES: MECHANISTIC CHARACTERISTICS IN THE PHOTOCHEMISTRY OF PYRIMIDO[5,4-g]PTERIDINE-10-OXIDE

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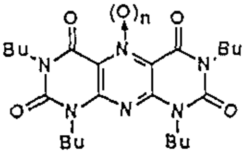
Abstract – *A novel heterocyclic N-oxide, pyrimido[5,4-g]pteridine-10-oxide (1), oxygenates cyclohexene (4) and norbornene (9) under the photochemical conditions to give the corresponding oxidation products, (5) - (8) and (10) - (12), respectively. Experimental results clearly indicate that the photochemical oxygenation by (1) involves a single-electron transfer from the olefins (4) and (9) to the singlet-excited (1) followed by oxygen-atom transfer rather than oxene mechanism.*

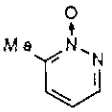
Our previous works [1] have demonstrated that a novel heterocyclic *N*-oxide, pyrimido[5,4-*g*]pteridine-10-oxide (**1**), [2] behaves as an agent for oxygenation or dehydrogenation under the photochemical conditions depending upon the nature of various aromatic substrates. The special features of the photooxidation by (**1**) are occurrence of the clean reaction not accompanied by appreciable intramolecular rearrangements of the *N*-oxide function [3] and possible involvement of an initial single-electron-transfer (SET) from the substrates to (**1**).

This work was undertaken to obtain mechanistic insights on the photochemistry of (**1**) upon choice of simple olefins, cyclohexene (**4**)($E^{ox}_{1/2}$: 2.14 V *vs* SCE) and norbornene (**9**)($E^{ox}_{1/2}$: 2.02 V *vs* SCE), [4] as favorite substrates.

In this communication, we wish to present substantial evidence supporting that the photooxygenation by (**1**) involves the initial SET from (**4**) and (**9**) to a singlet-excited (**1**), which is entirely different from the oxene mechanism proposed for the photooxygenation of olefins by some heterocyclic *N*-oxides, [3, 5-7] e.g., 3-methylpyridazine-2-oxide (**3**).



1, n = 1
2, n = 0



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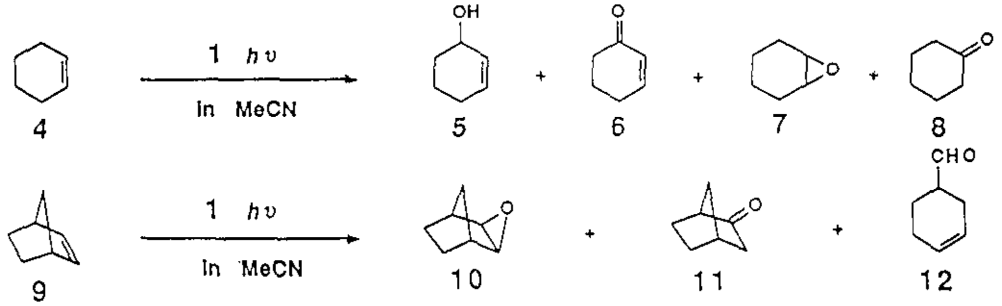

Scheme 1

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† This contribution is dedicated to the late Professor Tetsuji Kametani.

A mixture of (1)[5.0 mmol] and (4)[500 mmol] in dry acetonitrile was irradiated with uv-visible light through a Pyrex filter at ambient temperature under argon atmosphere for 40 min. During this period, about 40 % of (1) was deoxygenated to give pyrimido[5,4-*g*]pteridine (2) almost quantitatively. Cyclohexenol (5), cyclohexenone (6), epoxycyclohexane (7), and cyclohexanone (8) were obtained as oxygenated products in 23 %, 31 %, 2 %, and 2 % yields (based on the consumed 1), respectively. The yields and structures of these oxygenated products were determined by gc and gc-ms analyses.

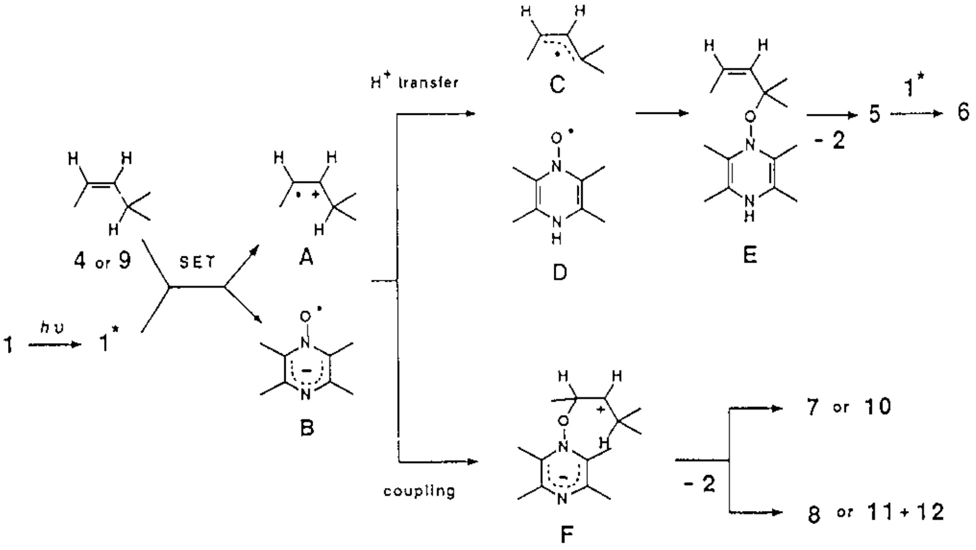
Experiments for the wavelength dependence showed that the formation of (5) occurs most efficiently by irradiation with around 365 nm lights which are near the longest uv absorption band of (1)[370 nm ($\varepsilon = 2.2 \times 10^4$)]. Quantum yield for the consumption of (1) was 0.014 under irradiation of a solution of (1)[5.0 mmol] and (4)[2.5 mol] in dry acetonitrile with 365 nm light.

In the photooxygenation of (4) by the pyridazine *N*-oxide (3) in methylene chloride, [6] the consumption rate of (3) has been found not to be affected by the presence of (4) in various concentrations, which has led to the hypothesis that an atomic oxygen (oxene) is liberated directly from the excited (3) and then intercepted by (4). [6] The analogous phenomenon was observed upon employment of acetonitrile as a solvent.

In sharp contrast, the photooxygenation of (4) by (1) showed evidently a concentration-dependence : the *N*-oxide (1) itself was quite stable in acetonitrile under the photochemical conditions, whereas the consumption of (1) was facilitated as the quantity of the added (4) increases, indicating that an interaction between (1) and (4) is a requisite for the photooxygenation. This discrepancy suggests that the present photooxygenation involves a reaction mode which is different from the oxene mechanism, frequently proposed for the photooxygenation by heterocyclic *N*-oxides. [3]

Additionally, the following facts are in agreement with above aspect : i) the pyridazine *N*-oxide (3) photochemically oxygenated cyclohexane to give cyclohexanol, supporting the generation of an oxene intermediacy. [5] The *N*-oxide (1), however, was very stable in cyclohexane under analogous conditions; ii) the product distribution in the photooxidation of (4) by (1) is different from the case of (3), i.e., in the case of (1), allylic oxidation of (4) to afford (5) and (6) occurred predominantly rather than epoxidation, while under our experimental conditions the photooxidation of (4) by (3) gave the epoxide (7)(17 %) and the cyclohexanone (8)(3 %) without the formation of the allylic oxidation products (5) and (6). [5,6]

The free energy change calculated for the SET from the electron donor (4) to the singlet-excited (1) (ΔG_{et} : -4.30 Kcal mol^{-1}) [8,9] suggests that the SET process is exothermic. The photooxygenation of (4) by (1) was significantly suppressed with a concentration dependence by addition of strong electron acceptors such as tetracyanoethylene and tetracyanoquinodimethane to the reaction medium. The Stern-Volmer plots for quenching of the fluorescence of (1) by (4) in acetonitrile were linear ($k_q \tau_s = 3.5$ M^{-1}) and the rate constant (k_q) was estimated to be *ca.* 1.2×10^9 M^{-1} s^{-1}, [10] which is near the diffusion controlled limit of 1×10^{10} M^{-1}s^{-1} in acetonitrile. These facts show that the present photooxygenation involves the initial SET from (4) to the singlet-excited (1) leading to cation- and anion-radicals, (**A**) and (**B**). (see Scheme 2)



Scheme 2

Radicals (**C**) and (**D**) could be formed by a proton transfer from (**A**) to (**B**). There have been precedents[11] for the analogous photoreactions involving the generation of the allyl radical (**C**) from cyclohexene (**4**) *via* sequent electron- and proton-transfers. The direct allylic hydrogen abstraction of (**4**) by a triplet-excited (**1**) leading to (**C**) [12] can be eliminated on the basis of the fact that neither a triplet sensitizer (acetone or acetophenone) nor a triplet quencher (diacetyl) had any significant effect on the formation of the allylic oxidation products (**5**) and (**6**). The radical coupling of (**C**) with (**D**) results in the formation of (**5**) and (**2**) *via* an intermediate (**E**). Subsequent dehydrogenation of (**5**) by the excited (**1**) gives (**6**). Coupling of the radical ions, (**A**) and (**B**), occurs to afford the epoxycyclohexane (**7**) and cyclohexanone (**8**) as a minor process *via* a zwitterionic intermediate (**F**). The coupling of photochemically generated radical cation-anion pair has been documented. [11, 13]

Under the analogous conditions, the photooxygenation of norbornene (**9**) by (**1**) resulted in the formation of *exo*-epoxynorbornane (**10**) and norcamphor (**11**) in 42 % and 4 % yields (by gc), respectively, together with a trace amount of cyclohexene-4-carboxaldehyde (**12**)(by gc and ^{1}H-nmr).

The calculated free-energy change (ΔG_{et} = -7.07 Kcal mol^{-1}) [8,9] and the quenching constant of the fluorescence of (**1**) by (**9**)(k_q = ca. 1.4 x 10^9 M^{-1} s^{-1}) suggest that the SET from (**9**) to the singlet-excited (**1**) occurs more easily than that from (**4**). In this case, however, the subsequent proton transfer from the cation radical (**A**) to the anion radical (**B**) leading to the allylic radical (**C**) is prevented due to the severe stereoelectronic hindrance. [14] As a consequence, the coupling of (**A**) with (**B**) occurs predominantly to give the epoxide (**10**) and the rearranged products (**11**) and (**12**) *via* an intermediate (**F**). (see Scheme 2)

The photoreaction of (**9**) by (**3**) under the analogous conditions resulted in the formation of (**10**) and (**11**) rather in poor yields (8 % and 1 %). The result obtained in a concentration-dependence experiment supports that this photoreaction could be operated by the oxene mechanism.

The hemin-catalyzed oxidation of (**4**) and (**9**),[15,16] a model reaction of cytochrome *P*-450, has been reported to give the oxygenated products (**5**) - (**8**), (**10**) - (**12**), and *endo*-epoxynorbornane.[17] The biological oxidation catalyzed by cytochrome *P*-450 can be best explained in most cases in terms of the initial SET from substrates to the oxidizing species symbolized by $(Fe^{IV} = O)^{+\cdot}$.[18] Thus we can conclude that the present photooxygenation of the simple olefins (**4**) and (**9**) by (**1**) well accommodates the hemin-catalyzed oxidation with respect to the involvement of the initial SET process.

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