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PHOTO-OXYGENATION OF ALKANES BY A HETEROCYCLIC N-OXIDE VIA NON-OXENE MECHANISM. PECULIAR PHOTOCHEMICAL PROPERTY OF PYRIMIDO[5,4-G]PTERIDINE N-OXIDE

Magoichi SAKO,* Kosaku HIROTA, and Yoshifumi MAKI *
Gifu Pharmaceutical University, 6-1, Mitahora-higashi 5-chome, Gifu 502, Japan

Irradiation of a solution of cyclohexane (**4**) or adamantane in chloroform containing pyrimido[5,4-g]pteridine N-oxide (**1**) with UV-visible light resulted in the formation of the corresponding oxygenated products together with chlorinated products. This indicates the occurrence of the chloroform-mediated radical reaction initiated by an excited **1**.

KEYWORDS photo-oxygenation; alkane; heterocyclic N-oxide; pyrimido[5,4-g]pteridine N-oxide; trichloromethyl radical; radical reaction

Photochemical oxygenation of alkanes by heterocyclic N-oxides such as 3-methylpyridazine N-oxide (**3**)[1, 2] and pyridine N-oxide[3] leading to the corresponding alcohols has provided a positive proof supporting liberation of an oxygen-atom in their triplet-excited states (the oxene mechanism).[4]

We have reported that pyrimido[5,4-g]pteridine N-oxide (**1**)[5] oxygenates cyclohexene[6] and benzenes[7] via a photo-induced single-electron transfer from these substrates to **1** (the SET mechanism). This is an alternative to the common oxene mechanism. In sharp contrast to **3** and pyridine N-oxide, **1** is quite stable in cyclohexane (**4**) as well as acetonitrile under UV-irradiation, providing strong chemical evidence in support of no oxene liberation from an excited **1**.[8]

This paper describes that when chloroform is used as a solvent the N-oxide **1** photochemically oxygenates the alkanes **4** and adamantane in a new way different from the oxene- or SET-mechanism. The present observation further demonstrates the peculiar photochemical property of **1** in comparison with the heterocyclic N-oxides **3** and pyridine N-oxide so far investigated and indicates that an excited **1** functions as a radical initiator and an oxygen-atom donor to the non-activated alkanes in chloroform.

A mixture of **1** [UV; λ_{max}: 370 ($\varepsilon = 2.2 \times 10^4$) nm] (5 mM) and **4** (1.85 M) in dry acetonitrile, methylene chloride, chloroform,[9] or carbon tetrachloride was irradiated with a 400 W high-pressure mercury arc lamp through a $BiCl_3$ solution filter (>355 nm) under argon for 3 h. Only in the case of chloroform was consumed a significant amount of **1** (75%) and was observed the formation of cyclohexanol (**5**)(37%), cyclohexanone (**6**) (12%), cyclohexylchloride (**7**)(11%), and hexachloroethane (**8**)(23%) together with pyrimido[5,4-g]pteridine (**2**)(36%) and some undetermined products originated from **1**.[10]

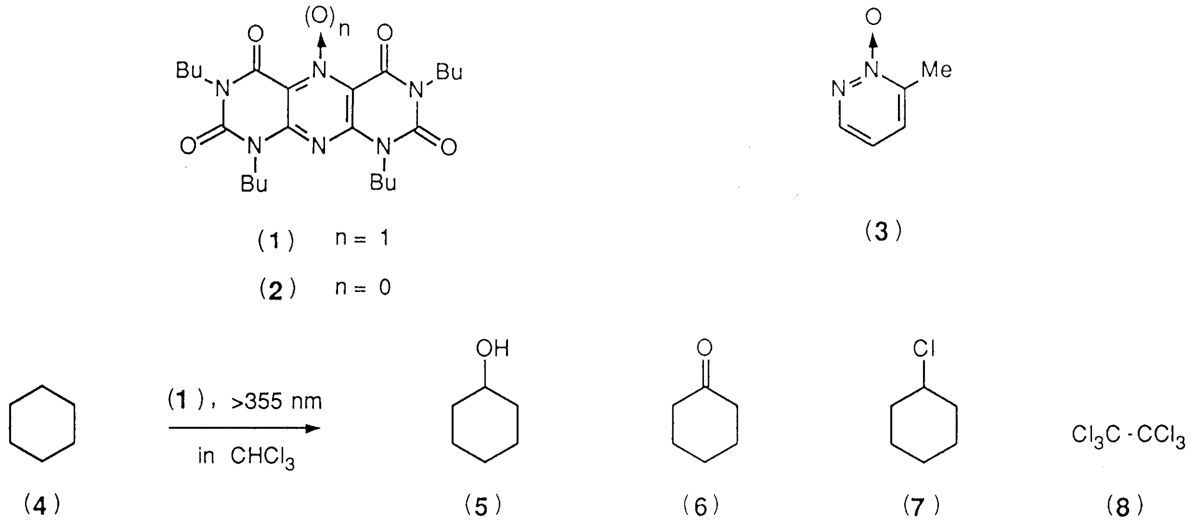

Chart 1

Contrary to the foregoing observations, when a mixture of **3** [UV;λ_{max}: 323 ($\varepsilon = 1.4 \times 10^4$)nm] (5 mM) and **4** (1.85 M) in the above four solvents was irradiated at around 323 nm (JASCO CRM-FA monochromator with 2 KW Xe lamp and 4 nm band width) for 10 min, **3** was completely consumed and the oxygenated products, **5** (25-37%) and **6** (5-19%), were obtained with independent of the nature of solvents. When chloroform was used, neither chlorinated product **7** nor **8** was formed.

Discrepancy in the solvent dependence and the product distribution between the photooxygenations of **4** by both _N_-oxides, **1** and **3**, shows clearly that **1** oxygenates **4** _via_ a reaction mode entirely different from the case of **3** (the oxene mechanism).

The reaction was complex, so we simplified a reaction sequence for the photoreaction of **4** with **1** in chloroform as shown in Chart 2.

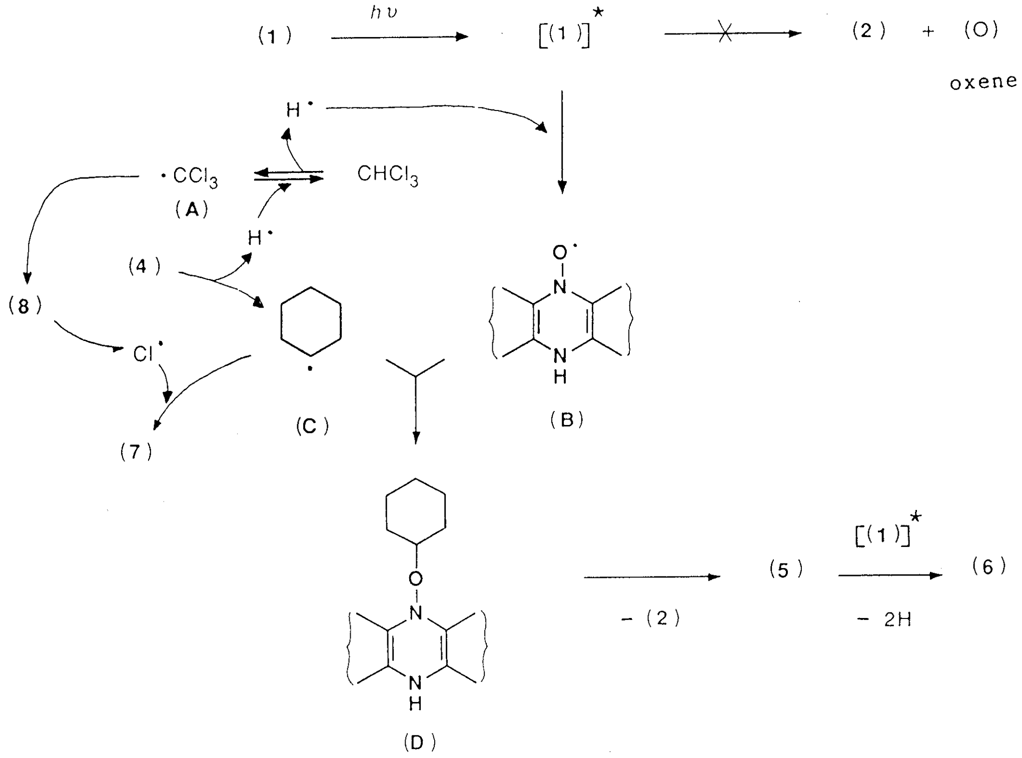

Chart 2

The capacity of the excited **1** [11] to abstract hydrogen is enough for chloroform but not for **4** [12] to generate the trichloromethyl radical (**A**) or the nitroxyl radical (**B**). Radical **A** readily abstracts hydrogen from **4** to give cyclohexyl radical (**C**) [13] and its generation accommodates the formation of the coupling product **8**. [14] A combination of the resulting radicals **B** and **C** leads to the formation of a transient intermediate (**D**) which then collapses to give **2** and **5**. Cyclohexanol (**5**) is oxidized _via_ hydrogen abstraction by the excited **1** or other radical species generated during the reaction to produce **6**. In fact, **5** was gradually converted into **6** by **1** under the photochemical conditions employed.

A significant amount of **7** is expected to be formed _via_ undetermined radical pathways. One possible pathway is the radical combination of **C** with a chlorine-atom from **8**. Chlorination of alkanes by polychlorinated hydrocarbons such as **8** in the presence of a radical initiator has been well documented. [15]

Only the oxygenated products **5** and **6** were formed in the photoreaction of **4** with **1** under aerobic conditions: when a mixture of **1** (5 mM) and **4** (500 mM) in dry chloroform was irradiated at >355 nm under air for 3 h, **5** (31%) and **6** (33%) were obtained but no **7** or **8** was formed. This can be rationalized in terms of efficient trapping of **A** and **C** by molecular oxygen.

Irradiation of a mixture of adamantane (500 mM) and **1** (5 mM) in dry chloroform at >355 nm under argon for 2 h gave 1-hydroxyadamantane (19%), 2-hydroxyadamantane (10%), 2-oxoadamantane (trace), 1-chloroadamantane (85%), 2-chloroadamantane (7%), and **8** (17%). The predominent formation of 1-chloroadamantane is surprising and the reason for it is not clear at present. Under the aerobic conditions, however, 1-hydroxyadamantane was produced in much improved yield (75%).

In summary, our results have shown that **1** oxidizes non-activated alkanes via a radical-chain pathway which is different from the oxene mechanism for oxygenation by the heterocyclic N-oxides studied previously.

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REFERENCES AND NOTES

1. H. Igeta, T. Tsuchiya, M. Yamada, and H. Arai, Chem. Pharm. Bull., **16**, 767 (1968); T. Tsuchiya, H. Arai, and H. Igeta, Tetrahedron Lett., **1969**, 2747.
2. Y. Ogawa, S. Iwasaki, and S. Okuda, Tetrahedron Lett., **22**, 2277 and 3637 (1981).
3. H. Strub, C. Strehler, and J. Streith, Chem. Ber., **120**, 355 (1987) and references cited therein.
4. For a recent review on the photochemistry of the heterocyclic N-oxides, see A. Albini and M. Alpegiani, Chem. Rev., **84**, 43 (1984).
5. Y. Maki, M. Sako, and E. C. Taylor, Tetrahedron Lett., **1971**, 4271; E. C. Taylor, Y. Maki, and A. McKillop, J. Org. Chem., **37**, 1601 (1972).
6. Y. Maki, M. Sako, T. Murase, Y. Kitade, and K. Hirota, Heterocycles, **30**, 279 (1990).
7. M. Sako, S. Ohara, K. Shimada, K. Hirota, and Y. Maki, J. Chem. Soc., Perkin Trans. 1, **1990**, 863.
8. For example, see M. Sako, K. Shimada, K. Hirota, and Y. Maki, J. Am. Chem. Soc., **108**, 6039 (1986).
9. Chloroform was freshly distilled after treatment with calcium chloride because consumption of **1** is significantly influenced on the presence of ethanol (an additive as stabilizer).
10. The structures of the photoproducts were confirmed by comparing their GC-retention times and GC-mass spectral data with the respective authentic samples. Yields are based on the consumed N-oxide **1** and are determined by GC and TLC densitometry.
11. The multiplicity of the excited **1** for the present photoreaction remains uncertain. A triplet-excited state, however, is favorable for it.
12. Energy for the C-H bond dissociation of chloroform is lower than that of methylene chloride, acetonitrile, and **4** (cf. V.I. Vedeneyev, L.V. Guroich, V.N. Kondrat'yev, V.A. Medvedev, and Y.L. Frankevich, " Bond Energies, Ionization Potentials, and Electron Affinities ", Edward Arnold Ltd., London, 1966).
13. K.U. Ingold, in " Free Radicals ", Ed. by J.K. Kochi, Weley-Interscience, N.Y., 1973, Vol. 1, Chapter 5.
14. Bicyclohexane and trichloromethylcyclohexane were not detected by GC-analysis. (cf. A. Ouchi, A. Yabe, Y. Inoue, Y. Daino, and T. Hakushi, J. Chem. Soc., Chem. Commun., **1989**, 1669; J. R. Lindsay Smith and Z. A. Malik, J. Chem. Soc., (B), **1970**, 617; A. Henglein, E. Heckel, Y. Ojima, and G. Meissner, Ber. Bunsenges. Physik. Chem., **67**, 988 (1963).
15. G.A. Russell, J. Org. Chem., **24**, 300 (1959); J. Nafisi-Movaghar and Y. Hatano, J. Phys. Chem., **74**, 1899 (1974); M.G. Katz, A. Horowitz, and L.A. Rajbenbach, Int. J. Chem. Kinet., **7**, 183 (1975); L. Saussine, E. Brazi, A. Robine, H. Mimoun, J. Fischer, and R. Weiss, J. Am. Chem. Soc., **107**, 3534 (1985) and references cited therein.

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