Communications to the Editor

[Chem. Pharm. Bull.]
[30(8)3028-3031(1982)]

PHOTO-DEAROMATIZATION.
1,2-PHOTOADDITION OF ALCOHOL TO N,3-DIMETHYLPHthalIMIDE
WITHOUT PHOTOENOLIZATION^{1,2)}

Yuichi Kanaoka,^{*,a} Yasumaru Hatanaka,^a Eileen N. Deusler,^b
Isabella L. Karle,^c and Bernhard Witkop^d

Faculty of Pharmaceutical Sciences, Hokkaido University,^a
Sapporo, 060 Japan, Department of Chemistry, University of
Illinois,^b Urbana, Illinois 61801, Laboratory for the Structure
of Matter, Naval Research Laboratory,^c Washington, D. C. 20375,
Laboratory of Chemistry, National Institute of Arthritis,
Metabolic & Digestive Diseases, National Institutes of Health,^d
Bethesda, Md. 20205, U. S. A.

Dearomatization of N,3-dimethylphthalimide occurs upon irradiation accompanying incorporation of the solvent alcohol in the aromatic ring. The X-ray crystal structure analysis of the product revealed the complete structure of a multi-substituted cyclohexene system. No evidence for formation of the photo-enol in the phthalimide system has been found during the study of the possible course of the photodearomatization.

KEYWORDS — photo-dearomatization; N,3-dimethylphthalimide; nucleophilic photoaddition; photoreduction; photoenolization; deuterium incorporation; X-ray analysis; 3a,4,5,7a-tetrahydro-4-alkyloxy-2,4-dimethyl-1H-isoindole-1,3(2H)-dione

One typical approach to overcome the resonance energy of benzenoids and to dearomatize them is by electronic excitation, a transformation for which there exist many precedents.³⁾ In this way various nucleophiles such as amine,⁴⁾ cyanide⁵⁾ and hydride⁶⁾ have been observed to add photochemically to benzenoids. Here we wish to report the photoaddition of alcohol: upon irradiation of N,3-dimethylphthalimide (1) in methanol, ethanol or isopropanol, 1,2-addition of alcohol resulted in dearomatization, without recourse to intermediate photoenolization.

In a typical example, irradiation (500 w high-pressure mercury lamp with a Pyrex filter, 8 h, N₂) of a 10 mM solution of (1) in methanol gave, besides two isomeric reduction products (2) (mixture, 27%) and addition products (3) (mixture, 30%), consistent with the general photochemical pattern of phthalimides,^{7,8)} a third compound (4a, mp 119-120°C, 14%), which was apparently formed by the addition of methanol to the benzene moiety of (1), followed by reduction.

Similarly, irradiation of (1) in ethanol and isopropanol led to the similar products (4b, mp 103-104°C) and (4c, mp 65-66°C),⁹⁾ while no detectable amount of the product was formed in *tert*-butanol. The results are summarized in Table I. The yields of the dearomatized products (4) increase in the order of reactivity of the α -hydrogen of alcohols to hydrogen abstraction.

2a: Y=H

3a: Y=CH₂OH

2b: Y=H

3b: Y=CH₂OH

Table I. Yields of 4 in Various Alcohols

Solvent	Time (h)	R	<u>4</u>	X	Yield (%)
MeOH	8	<u>a</u>	CH ₃	H	14
EtOH	1	<u>b</u>	CH ₃ CH ₂	H	27
<i>iso</i> -PrOH	1	<u>c</u>	(CH ₃) ₂ CH	H	31
<i>tert</i> -BuOH	8	-	-	-	-
MeOD	50	<u>d</u>	CH ₃	D	3
EtOD	8	<u>e</u>	CH ₃ CH ₂	D	5

The complete structure and the stereoconfiguration at the three new asymmetric centers of (4b) was established by X-ray analysis. The crystal structure analysis of (4b) confirmed the *cis* ring-junction and that the CH₃ group on C-4 is on the same side as the *cis* hydrogen atom on C-3a and C-7a. The name of the compound is 3a β ,4,5,7a β -tetrahydro-2,4 β -dimethyl-4 α -ethoxy-1H-isoindole-1,3(2H)-dione. Bond lengths and angles are shown in Fig. 1. The conformation of the molecule has the following features: an equatorial CH₃ and an axial O-ethyl *trans* to C-3a and a dihedral angle of 135° between the planes of the two rings.¹⁰⁾

The imide (1) possesses two imide carbonyls, one of which is formally photo-enolizable, and the other is not. One attractive explanation for the formation of (4) could be addition of alcohol to a photo-generated enol (5→8). When (1) was thermally reduced with sodium borohydride, the isomer ratio of (2a) and (2b) was approximately equal to the value (3 : 2) observed in the above photoreaction. So there seems to be no significant intramolecular photoenolization in competition with intermolecular photoreduction.¹¹⁾

To confirm this, photolysis of (1) in CH₃OD or CH₃CH₂OD was examined (Table I). Based on pmr spectrometry, the recovered imide (1) incorporated no detectable amount of deuterium at the aromatic methyl group. By contrast, the products (4d) and (4e) were found to contain significant amounts of deuterium at the ring fused carbons: (4d) contained nearly quantitative and ca. 60% deuterium, at the 3a position and at the 7a position, respectively.

A plausible mechanism of the photo-dearomatization reaction is illustrated in Chart 1. Initial 1,2- and 1,4-addition of alcohol to an excited state ben-

zenoid (6) including the conjugated imide carbonyls affords (7) and (8), respectively, and the latter will readily lead to its keto-form (7).¹²⁾ Photoreduction of the dienone by hydrogen abstraction from the α -H in alcohols (no α -H in tert-butanol) gives rise to (9), followed by the reversion of the enol (9) to the keto-form (4) resulting in partial incorporation of solvent deuterium at C-7a.

Chart 1

A number of photochemical aromatic substitutions have been reported including nucleophilic substitution with alkoxy groups.¹³⁾ Photoaddition of alcohols to double bonds in olefin¹⁴⁾ and enone¹⁵⁾ is also well known. However, nucleophilic photoaddition of alcohols to benzenoids has not been reported. It is worth noting that in a multi-substituted benzenoid system such as (1), the addition of alcohol to a benzene moiety effectively competes with the usual addition to a carbonyl. The scope and limitation of this dearomatization reaction, both with regard to substrates and addends, are under investigation.

ACKNOWLEDGEMENT This work was supported in part by a grant in aid (to Y. K.) from the International Cooperation Program of the Japan Society for the Promotion of Science, which is gratefully acknowledged.

REFERENCES AND NOTES

- 1) Photochemistry of the Phthalimide System. 29. Part 28: M. Machida, H. Takechi, Y. Shishido and Y. Kanaoka, submitted.
- 2) Photoinduced Reactions. 58. Part 57: M. Machida, S. Oyadomari, H. Takechi, K. Ohno and Y. Kanaoka, submitted.
- 3) D. Bryce-Smith, *Pure Appl. Chem.*, **34**, 193 (1973).
- 4) a) N. C. Yang and J. Libman, *J. Am. Chem. Soc.*, **95**, 5783 (1973); b) D. Bruce-

- Smith, A. Gilbert and C. Manning, *Angew. Chem. Internat. Edit.*, 13, 314 (1974); and references cited therein.
- 5) M. Masuda, C. Pac and H. Sakurai, *J. Chem. Soc., Perkin I*, 1981, 746.
 - 6) M. Masuda, C. Pac and H. Sakurai, *J. Org. Chem.*, 46, 788 (1981).
 - 7) Y. Kanaoka and K. Koyama, *Tetrahedron Lett.*, 1972, 4517.
 - 8) Y. Kanaoka, *Accounts Chem. Res.*, 11, 407 (1978).
 - 9) All new compounds gave satisfactory elemental analyses and spectral properties (ir, nmr, mass) consistent with the assigned structures.
 - 10) A six-membered ring with five atoms except C-4 lies in a plane, and a five membered ring is essentially coplanar with the two carbonyl oxygens and the N-methyl carbon.
 - 11) P. G. Sammes, *Tetrahedron*, 32, 405 (1976).
 - 12) If the 1,2-addition is assumed to proceed in a *cis* mode,¹⁵⁾ the *trans* stereochemistry of the products (4, and therefore, 7) suggests that the 1,4-addition is predominant. However, both pathways are tentatively included.
 - 13) J. Cornelisse and E. Havinga, *Chem. Rev.*, 75, 353 (1975).
 - 14) J. A. Marshall, *Accounts Chem. Res.*, 2, 33 (1969).
 - 15) D. I. Schuster, "Rearrangements in Ground and Excited States", (ed. by P. de Mayo) Academic Press, New York, vol 3, p. 181 (1980).

Fig. 1. Bond Lengths and Angles of 4b

(Received June 2, 1982)