Chem. Pharm. Bull. 26(3) 989—992 (1978)

UDC 547.584.04 : 541.14.04

Photochemistry of the Phthalimide System. XVI.[1] Photocyclization of N-Methylenebisphthalimides[2]

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(Received July 21, 1977)

Photolysis of N-methylenebisphthalimides (**6**) gave the intramolecularly cyclized compounds (**7**), products of recombination of ketyl-like intermediates which are not obtained in usual intermolecular reactions.

Keywords——bichromophoric system; ketyl-like radical; Norrish type II process; intramolecular radical coupling; radical transfer

In our systematic studies on the photochemistry of the phthalimide system, the imide carbonyl group of N-substituted phthalimides was found to behave photochemically like the carbonyl group of simple ketone systems undergoing such reactions as γ or δ hydrogen abstraction (Norrish Type II). For example, photocyclization, photoreduction and photoaddition of N-substituted phthalimides have been extensively studied.[4]

It is well known that aromatic ketones in the n, π^* triplet state abstract hydrogen from solvent and yield pinacols by a ketyl radical recombination reaction. On excitation phthalimides (**1**) are also thought to react in the triplet state;[4] however, the ketyl-like radical (**2**) which is assumed to form as the intermediate[4] does not lead to the formation of the corresponding pinacol (**3**), usually affording addition-(**4**) or cyclization-products (**5**) (Chart 1). This difference in photochemical behavior has not yet been clearly understood. In the present work we investigated this problem through photolysis of several N-methylenebisphthalimides (**6**) because the intramolecular reaction of these bichromophoric substrates would be expected to favor the pinacol formation.

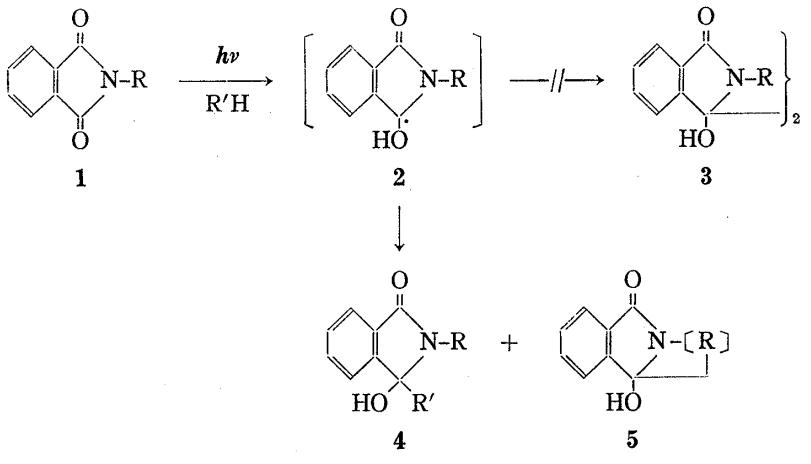


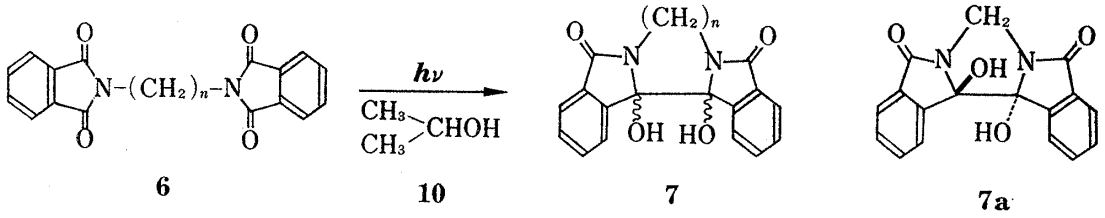
Chart 1

1) Part XV: M. Terashima, K. Koyama, and Y. Kanaoka, *Chem. Pharm. Bull.* (Tokyo), **26**, 630 (1978).
2) Photoinduced Reaction. XXX. Part XXIX: Y. Kanaoka, K. San-nohe, K. Itoh, Y. Hatanaka, M. Machida, and M. Terashima, *Heterocycles*, **6**, 29 (1977).
3) Location: *Kita-12, Nishi-6, Kita-ku, Sapporo, 060, Japan.*
4) *a*) Y. Kanaoka and K. Koyama, *Tetrahedron Lett.*, **1972**, 4517; *b*) Y. Kanaoka, Y. Migita, K. Koyama, Y. Sato, H. Nakai, and T. Mizoguchi, *ibid.*, **1973**, 1193; *c*) Y. Sato, H. Nakai, H. Ogiwara, T. Mizoguchi, and Y. Kanaoka, *ibid.*, **1976**, 1889 and papers cited therein.

N-Methylenebisphthalimides (**6**) were irradiated with a 100 watt high pressure mercury arc in warm 2-propanol (**10**), a good hydrogen-donating solvent. As expected, the intramolecular coupling products (**7a—c**) were obtained, respectively, in the case of **6a—c**, with small amount of the reduced products (**9**). However, compounds (**6d, e**) in which the two phthalimide moieties are separated by four or more of methylene groups did not afford the coupling product, giving only the reduced products (**8** and **9**). These results are shown in Table I and Chart 2. The structural assignment of these products were made on the basis of elemental analyses and their spectral properties. For the five-membered ring compound (**7a**), the nuclear magnetic resonance (NMR) spectrum showed a singlet peak for a methylene in support of the *trans* diol structure, since the examination of the molecular model indicates that for the *cis* isomer the nonequivalent two protons must show a splitting pattern. For the other larger ring compounds (**7b, c**) the stereochemistry remained undetermined.

Table I. Yields of the Photoproducts

Compound (6)		Yield (%)			
	n	7	8	9	6 (recovered)
a	1	14	—	9	Trace
b	2	19	—	3	4
c	3	16	—	—	5
d	4	—	5	8	Trace
e	5	—	5	5	4



6 **10** **7** **7a**

8 **9**

a: $n=1$ b: $n=2$ c: $n=3$ d: $n=4$ e: $n=6$

Chart 2

In analogy with the benzpinacol formation from benzophenone, formation of the cyclized products (**7a—c**) can be rationalized on the basis of initial hydrogen abstraction by the imide carbonyl from 2-propanol giving a ketyl radical (**11**), followed by the second abstraction by the other phthalimide to form a di-ketyl radical (**14**), and coupling of the diradical (Chart 3). Another pathway is also possible. The initially formed ketyl radical (**11**) may intramolecularly add[5] to the imide carbonyl double bond to give an alkoxy radical (**13**) which then abstracts hydrogen from the medium. In either way of the above, the cyclization process (**14**→**7** or **11**→**13**) is less favorable for the longer chain compounds (**6d, e**).

Regardless to the details of the mechanism, it is worth noting that ketyl-like radicals derived from phthalimides are capable of recombination at least under the intramolecular

5) W.A. Pryor, "Free Radicals," McGraw-Hill, New York, 1966, p. 201, 277.

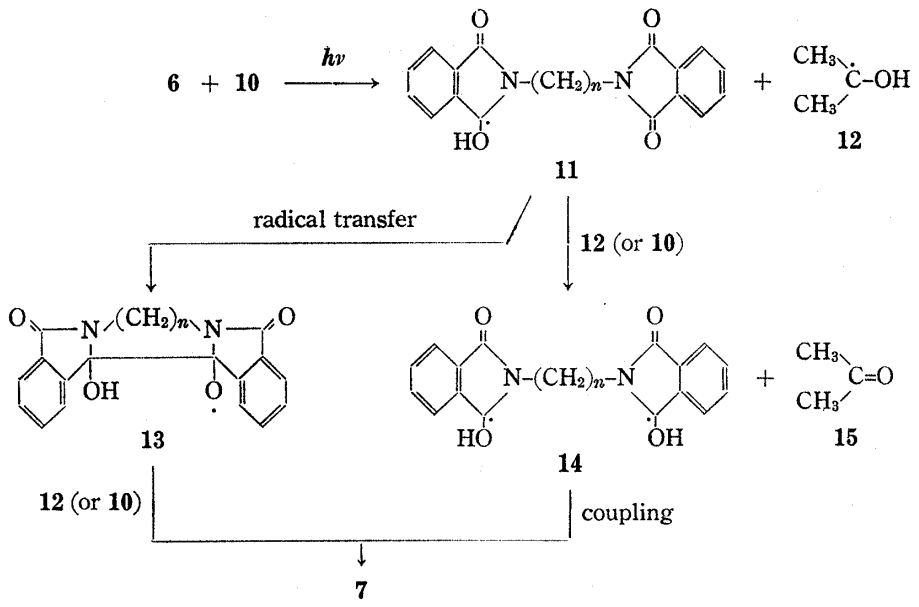


Chart 3

conditions. Photochemistry of non-conjugated bichromophoric systems has recently attracted considerable attention because incorporation of two chromophores into a molecule can change the photochemical properties of each of the chromophores.[6] However inspection of the ultraviolet (UV) spectra of **6** revealed that there exist no substantial interactions between the two phthalimide groups at least in the ground states. Therefore the major factor operating to control the coupling reaction may be a probability to form a productive complex by intramolecular special arrangement of the participating groups within life times of the intermediates. Recently Szwarc, *et al.*[7] prepared anion radicals of the bisphthalimides including **6b**—**e** and studied the methylene chain flexibility through kinetics of intramolecular electron transfer. Search for combination of more effective acceptor and donor pairs including a phthalimide, such as phthalimide and aromatic amines, is under way and will be published in a forthcoming paper.[8]

Experimental

Melting points were taken on a Yamato melting point apparatus and are uncorrected. Infrared spectrum (IR) was recorded with JASCO DS 701G infrared spectrometer. NMR spectra were all measured using a Hitachi Model R-20B high resolution NMR spectrometer. Signals are reported in ppm from tetramethylsilane as an internal standard. Mass spectra (MS) were obtained with a Model RMU-7E Hitachi mass spectrometer. Light source was an Type PIH-100 (Eikosha, Osaka) 100 watt high pressure mercury lamp.

N-Methylenebisphthalimides (6a—e)——Compounds (**6a, d, e**) were obtained from N-potassium phthalimide with diiodomethane, tetramethylenedibromide, and pentamethylenedibromide, respectively, by warming at 150° for 10—30 min in dimethylformamide. Compounds (**6b** and **6c**) were obtained from phthalic anhydride with ethylenediamine and propanediamine, respectively, by warming at 150° for 30 min then 200° for 30 min. Recrystallized from dimethylformamide, **6a**, mp 228—229° (lit.,[9] mp 232°). **6b**, mp 235—236° (lit.,[9] mp 236°). **6c**, mp 198—199° (lit.,[9] mp 198°). **6d**, mp 226—227° (lit.,[9] mp 227°). **6e**, mp 186—187° (lit.,[9] mp 188°).

General Procedure of Irradiation——A solution of **6** (1 mmol) in 200 ml of warm 2-propanol (5 mM) was irradiated for 30 min with a 100 watt high pressure mercury lamp. First and second run were combined, and the solvent was removed under reduced pressure. The residue was purified with preparative thin-layer chromatography (TLC) (Wakogel B-5F), followed by recrystallization of each fraction as appropriate.

6) F.C. DeSchryver and J. Put, *Ind. Chim. Belg.*, **1972**, 1107.
7) K. Shimada, Y. Himozato, and M. Szwarc, *J. Am. Chem. Soc.*, **97**, 5834 (1975).
8) M. Machida, H. Takechi, and Y. Kanaoka, *Heterocycles*, **7**, 273 (1977).
9) G. Vanag, *Ber.*, **75B**, 719 (1942).

Diisoindolono[2′,3′-c; 3″,2″-e]imidazolidine-4,5-diol (7a) and N-Methylenebis-3-hydroxyisoindol-1-one (9a) from 6a (*n*=1)——The products were separated from the starting material with TLC (AcOEt), then recrystallized from AcOEt to give **7a** (1st crop) and **9a** (2nd crop). **7a**, colorless prisms of 86 mg (14%), mp 230—232°. MS *m/e*: 308 (M^+). NMR (DMSO-d_6) δ: 4.94 (2H, singlet, $-CH_2-$), 7.09 (2H, singlet, –OH), 7.69 (8H, singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3440 (OH), 1690 (C=O). Diisoindolono[2′,3′-*c*; 3″,2″-*e*]imidazolidine-4,5-diol (**7a**): *Anal.* Calcd. for $C_{17}H_{12}N_2O_4$: C, 66.23; H, 3.92; N, 9.09. Found: C, 66.13; H, 3.94; N, 8.88. **9a**, colorless needles of 56 mg (9%). mp 198—200° MS *m/e*: 292 (M^+-18). NMR (DMSO-d_6) δ: 5.23 (2H, singlet, $-CH_2-$), 5.96 (2H, doublet, J=6 Hz, CHOH), 6.63 (2H, doublet, J=6 Hz, –OH), 7.64 (8H, multiplet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3280 (OH), 1685 (C=O). N-Methylenebis-3-hydroxyisoindole-1-one (**9a**): *Anal.* Calcd. for $C_{17}H_{14}N_2O_4$: C, 65.80; H, 4.45; N, 9.03. Found: C, 65.82; H, 4.57; N, 8.93.

Diisoindolono[2′,3′-a; 3″,2″-c]piperazine-5,6-diol (7b) and N-Ethylenebis-3-hydroxyisoindol-1-one (9b) from 6b (*n*=2)——TLC was developed with AcOEt–CH_2Cl_2 (2: 1). **7b** was recrystallized from MeOH, colorless prisms of 122 mg (19%), mp 270—272°. MS *m/e*: 322 (M^+). NMR (DMSO-d_6) δ: 3.12 (2H, doublet, J=9 Hz, $-CH\underline{CH}-$), 4.16 (2H, doublet, $-CH\underline{CH}-$), 6.72 (2H, singlet, –OH), 7.73 (8H, broad singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3400 (OH), 1665 (C=O). Diisoindolono[2′,3′-*a*; 3″,2″-*c*]piperazine-5,6-diol: *Anal.* Calcd. for $C_{18}H_{14}N_2O_4$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.17; H, 4.44; N, 8.68. **9b** was recrystallized from AcOEt, colorless needles of 22 mg (3%), mp 181—184°. MS *m/e*: 306 (M^+-18). NMR (DMSO-d_6) δ: 3.86 (4H, singlet, $-C\underline{H}_2C\underline{H}_2-$), 5.97 (2H, broad singlet, $-C\underline{H}$), 6.35 (2H, broad singlet, –OH), 7.55 (8H, singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3400 (OH), 1690 (C=O). N-Ethylenebis-3-hydroxyisoindole-1-one (**9b**): *Anal.* Calcd. for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.40; H, 5.08; N, 8.56.

Diisoindolono[2′,3′-a; 4″,3″-c]homopiperazine-2,3-diol (7c) from 6c (*n*=3)——TLC was developed with AcOEt–CH_2Cl_2 (2: 1). **7c** was recrystallized from MeOH, colorless prisms of 106 mg (16%), mp 198—199°. MS *m/e*: 336 (M^+). NMR (DMSO-d_6) δ: 2.08 (2H, quintet, J=6 Hz, $-CH_2C\underline{H}_2CH_2-$), 3.13 and 3.36 (2H, two of triplet, J=6 Hz, $-C\underline{H}CH_2C\underline{H}-$), 3.85 and 4.09 (2H, two of triplet, J=6 Hz, $-C\underline{H}CH_2C\underline{H}-$), 6.78 (2H, singlet, –OH), 7.2—7.8 (8H, multiplet, aromatic protons); by irradiation at δ 2.08, 3.23 (2H, doublet, J= 14 Hz) and 3.97 (2H, doublet, J=14 Hz) instead of 3.13, 3.36, 3.85 and 4.09. IR ν_{max}^{Nujol} cm^{-1}: 3160 (OH), 1670 (C=O). Diisoindolono[2′,3′-*a*; 4″,3″-*c*]homopiperazine-2,3-diol (**7c**): *Anal.* Calcd. for $C_{19}H_{16}N_2O_4$: C, 67.85; H, 4.80; N, 8.33. Found: C, 67.71; H, 4.88; N, 8.35.

2-(N-Phthalyl-δ-aminobutyl)-3-hydroxyisoindol-1-one (8d) and N-Butylenebis-3-hydroxyisoindol-1-one (9d) from 6d (*n*=4)——TLC was developed twice with AcOEt–CH_2Cl_2 (2: 1). **8d** was recrystallized from AcOEt, colorless fine needles of 22 mg (5%), mp 212—214°. MS *m/e*: 350 (M^+). NMR (DMSO-d_6) δ: 1.62 (4H, multiplet, $-CH_2(C\underline{H}_2)_2CH_2-$), 3.60 (4H, multiplet, $-C\underline{H}_2(CH_2)_2C\underline{H}_2-$), 5.78 (1H, doublet, J=9 Hz, –CH), 6.52 (1H, doublet, J=9 Hz, –OH), 7.55 (4H, singlet, aromatic protons), 7.80 (4H, singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3280 (OH), 1765, 1720, 1670 (C=O). 2-(N-phthalyl-δ-aminobutyl)-3-hydroxyisoindol-1-one (**8d**): *Anal.* Calcd. for $C_{20}H_{18}N_2O_4$: C, 68.56; H, 5.18; N, 8.00. Found: C, 68.51; H, 5.14; N, 7.85. **9d** was recrystallized from MeOH, colorless fine needles of 58 mg (8%), mp 206—208°. MS *m/e*: 334 (M^+-18). NMR (DMSO-d_6) δ: 1.66 (4H, broad singlet, $-CH_2(C\underline{H}_2)_2CH_2-$), 3.50 (4H, multiplet, $-C\underline{H}_2(CH_2)_2C\underline{H}_2-$), 5.78 (2H, doublet, J=9 Hz, –OH), 7.58 (8H, singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3280 (OH), 1665 (C=O). N-butylenebis-3-hydroxyisoindol-1-one (**9d**): *Anal.* Calcd. for $C_{20}H_{20}N_2O_4 \cdot 1/4H_2O$: C, 67.34; H, 5.75; N, 7.85. Found: C, 67.48; H, 5.79; N, 7.81.

2-(N-Phthalyl-ε-aminopentyl)-3-hydroxyisoindol-1-one (8e) and N-Pentylbis-3-hydroxyisoindol-1-one (9e) from 6e (*n*=5)——TLC was developed with AcOEt–CH_2Cl_2 (1: 1). **8e** was recrystallized from AcOEt, colorless fine needles of 38 mg (5%), mp 143—144°. MS *m/e*: 364 (M^+). NMR (DMSO-d_6) δ: 1.56 (6H, multiplet, $-CH_2(C\underline{H}_2)_3CH_2-$), 3.58 (4H, multiplet, $-C\underline{H}_2(CH_2)_3C\underline{H}_2-$), 5.82 (1H, doublet, J=9 Hz, –OH), 7.58 (4H, singlet, aromatic protons), 7.84 (4H, singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3300 (OH), 1765, 1718, 1675 (C=O). 2-(N-Phthalyl-ε-aminopentyl)-3-hydroxyisoindol-1-one (**8e**): *Anal.* Calcd. for $C_{21}H_{20}N_2O_4$: C, 69.21; H, 5.53; N, 7.69. Found: C, 69.13; H, 5.60; N, 7.68. **9e** was recrystallized from AcOEt, colorless fine needles of 36 mg (5%), mp 167—169°. MS *m/e*: 366 (M^+). NMR (DMSO-d_6) δ: 1.0—2.0 (6H, multiplet, $-CH_2(C\underline{H}_2)_3CH_2-$), 3.1—3.8 (4H, multiplet, $-C\underline{H}_2(CH_2)_3C\underline{H}_2-$), 5.82 (2H, doublet, J=9 Hz, –CH), 6.53 (2H, doublet, J=9 Hz, –OH), 7.57 (8H, singlet, aromatic protons). IR ν_{max}^{Nujol} cm^{-1}: 3260 (OH), 1675 (C=O). N-Pentylbis-3-hydroxyisoindol-1-one (**9e**): *Anal.* Calcd. for $C_{21}H_{22}N_2O_4$: C, 68.83; H, 6.05; N, 7.65; Found: C, 68.56; H, 6.11; N, 7.44.

Acknowledgement This work was supported by a Grant-in-aid for Scientific Research from the Ministry of Education, Science and Culture.