Photochemistry of *N*-But-3-enyl Thiophthalimides.[1] Intramolecular Thietane Formation

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Upon irradiation, *N*-but-3-enyl thiophthalimides 7 undergo intramolecular Paterno–Büchi-like cycloaddition to give thioimide-thietanes, which are also photochemically converted into pyridoisoindolones 9.

Keywords photochemistry; *N*-but-3-enyl thiophthalimide; pyridoisoindolone; γ-hydrogen abstraction; intramolecular thietane formation; Paterno–Büchi; NOE

In our general study on the photochemistry of thioimide systems,[3] we have found that the thioimides efficiently undergo photocycloaddition (Paterno–Büchi-like reaction), but seem substantially inert to the Norrish type I and II processes. In addition, since it has been found that certain cyclic thioimides having an *N*-ω-phenylalkyl substituent undergo the Norrish type II cyclization,[4] we have investigated competition between the Norrish type II and Paterno–Büchi-like reaction.[5]

As a logical extension of our program, photoreaction of *N*-3-alkenylthiophthalimides (two methylenes) was investigated, and the result was the formation of pyridoisoindolone. Similarly, Coyle and Rapley have reported that photoreaction of *N*-(4-phenylbut-3-enyl)thiophthalimide afforded a pyridoisoindolone.[6] The proposed mechanistic process was pathway A *via* γ-hydrogen abstraction as shown in Chart 1. However, the results of our systematic research on the photoreaction of this system raise a question concerning the involvement of γ-hydrogen abstraction.

In order to assess the generality of this reaction process we chose simple *N*-but-3-enylthiophthalimide derivatives **7**. Irradiation of **7a** ($R^1=R^2=R^3=H$) afforded the pyridoisoindolone structure **9a** as a single product (74%) (Table

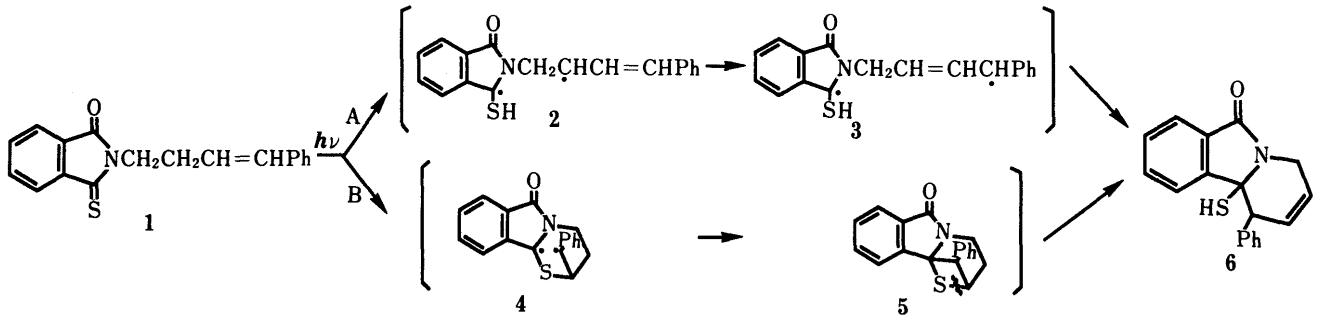

Chart 1

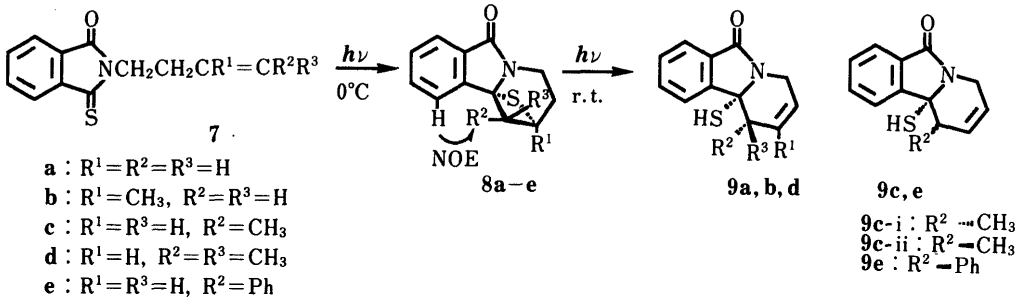

Chart 2

TABLE I. Photoreactions of 7 at Room Temperature

Thioimide	Product	Yield (%)	Appearance[a]	mp (°C)	Formula	Analysis (%) Calcd C	H	N	S	Found C	H	N	S
7a	**9a**	74	Colorless plates	104—105.5	$C_{12}H_{11}NOS$	66.35	5.10	6.45	14.73	66.48	5.39	6.59	14.72
7b	**9b**	84	Colorless plates	101—102.5	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84	67.63	5.89	5.92	13.59
7c	**9c-i**	38	Colorless plates	108.5—110	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84	67.78	5.39	5.88	13.61
	9c-ii	39	Colorless plates	116—117.5	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84	67.48	5.54	6.34	13.59
7d	**9d**	72	Colorless plates	123—125	$C_{14}H_{15}NOS$	68.55	6.16	5.71	13.05	68.61	6.22	5.57	13.27

a) Recrystallized from *n*-hexane–ethyl acetate.

I). Similarly, upon irradiation **7b—d** afforded pyridoisoindolone derivatives (**9b—d**, respectively) (Chart 2).

The structures of the photoproducts (**9**) were assigned on the basis of elemental analyses and spectral data. The mass spectrum (MS) of **9a** showed the molecular ion peak ($M^+=217$), and a significant fragment peak (M^+-34) corresponding to the loss of hydrogen sulfide from the molecular ion. In the proton nuclear magnetic resonance (^{1}H-NMR) spectra, **9a—d** showed some multiplet peaks except for the peaks due to the thiol and methyl groups. The signal of the methyl group for **9c**-ii (0.50 ppm) appeared in the upfield region compared with that for **9c**-i (1.40 ppm). This can be explained on the basis of the anisotropic effect of the phenyl ring on the isoindole moiety, suggesting that the thiol group and the methyl group are in a *trans* relationship for **9c**-ii and *cis* for **9c**-i. The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectra of **9** showed the presence of a newly formed quaternary carbon (146.8—150.0 ppm) substituted by a thiol group, instead of a thiocarbonyl.

In all photoreactions, when the progress of reactions was monitored by thin layer chromatography (TLC), a new spot due to a labile intermediate was observed. In order to isolate the intermediate, irradiation of **7a** was performed at low temperature (0°C). As expected, **8a** (63%) was obtained accompanied with the pyridoisoindolone **9a** (20%). The structure of **8a** was assigned on the basis of the spectral data. The ^{1}H-NMR spectrum of **8a** showed a multiplet at 3.75 (1H, SCH), a triplet at 3.40 (1H, SCH-C$\underline{H}_2$) and a doublet of doublets at 2.75 (1H, SCH-C$\underline{H}_2$), but no signal due to a thiol group, and the structure was assigned as the thietane **8a** based on ^{1}H-decoupling experiments. Similarly, **7b—d** afforded thietanes **8b—d** and isoindolones **9b—d** (Table II). The stereochemistry of **8c** was determined on the basis of the nuclear Overhauser enhancement (NOE) analysis. Irradiation of the indicated benzene proton gave a slight enhancement (4.2%) of the intensity of the methyl (R^2) signal. Presumably the isoindolones were derived by photochemical ring fission from the initially formed thietanes. In fact, thietanes **8a—d** were easily converted to pyridoisoindolones **9a—d** by irradiation at room temperature. Therefore, the proposed pathway B for the formation of isoindolones **9** was supported by isolation of the intermediates **8** (Chart 2). To confirm this reaction pathway further, the same substrate **7e** as reported by Coyle and Rapley[6] was irradiated under similar conditions to those

Table II. Photoreactions of **7** at 0°C

Thioimide	Product	Yield (%)	Appearance	Formula	Analysis (%) Calcd (Found) C	H	N	S
7a	**8a**	63	Yellow oil	$C_{12}H_{11}NOS$	66.35	5.10	6.45	14.73
	9a	20			(66.56	5.13	6.34	14.89)
7b	**8b**	51	Yellow oil	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84
	9b	32			(67.59	5.48	5.99	13.79)
7c	**8c**	48	Yellow oil	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84
	9c-i	11			(67.33	5.87	6.21	13.93)
	9c-ii	13						
7d	**8d**	52	Yellow oil	$C_{14}H_{15}NOS$	68.55	6.16	5.71	13.05
	9d	29			(68.73	6.43	5.94	13.11)
7e	**8e**	24	Yellow oil	$C_{18}H_{15}NOS$	73.52	5.18	4.84	10.93
	9e[6]	14			(73.67	5.41	4.69	11.08)

Table III. Spectral Data for Photoproducts (**8**, **9**)

Compound	IR (cm^{-1})	MS (m/z)	^{1}H-NMR ($CDCl_3$) δ	^{13}C-NMR ($CDCl_3$) δ
8a	1670	217 (M^+)	2.00 (2H, m), 2.75 (1H, dd, J=4, 9 Hz), 3.40 (1H, t, J=9 Hz), 3.75 (1H, m, SCH), 3.95, 4.30 (2H, m), 7.2—7.9 (4H, m, aromatic protons)	22.3 (t), 35.0 (t), 40.6 (t), 48.8 (d), 65.0 (s), 122.6 (d), 123.5 (d), 128.8 (d), 131.7 (s), 132.2 (d), 149.2 (s), 168.5 (s)
8b	1670	231 (M^+)	1.35 (3H, s), 2.15 (2H, m), 2.75 (1H, d, J=9 Hz), 3.40 (1H, d, J=9 Hz), 3.95, 4.30 (2H, m), 7.2—7.9 (4H, m, aromatic protons)	18.2 (q), 28.5 (t), 35.2 (t), 41.7 (t), 52.3 (s), 64.8 (s), 121.9 (d), 123.8 (d), 129.1 (d), 131.0 (s), 133.5 (d), 146.7 (s), 168.7 (s)
8c	1670	231 (M^+)	1.25 (3H, d, J=6 Hz), 2.15 (2H, m), 2.70 (1H, m), 3.75 (1H, m), 3.95, 4.30 (2H, m), 7.2—7.9 (4H, m, aromatic protons)	17.9 (q), 24.5 (t), 36.8 (d), 41.2 (t), 48.7 (d), 65.5 (s), 121.4 (d), 124.0 (d), 130.2 (d), 131.5 (s), 133.4 (d), 146.0 (s)
8d	1670	245 (M^+)	1.25 (3H, s), 1.35 (3H, s), 2.10 (2H, m), 3.80 (1H, m), 3.95, 4.35 (2H, m), 7.2—7.8 (4H, m, aromatic protons)	18.2 (q), 19.5 (q), 25.3 (t), 37.2 (d), 43.5 (t), 47.9 (s), 66.3 (s), 122.1 (d), 125.1 (d), 130.8 (d), 132.7 (s), 133.9 (d), 147.4 (s), 168.4 (s), 168.9 (s)
8e	1670	293 (M^+)	2.10 (2H, m), 3.65 (1H, m), 3.75 (2H, m), 3.95, 4.35 (2H, m), 7.0—7.9 (9H, m, aromatic protons)	26.0 (t), 38.1 (d), 40.2 (t), 42.3 (d), 65.2 (s), 122.3 (d), 122.9 (d × 2), 125.3 (d × 2), 125.8 (d), 130.5 (d), 131.9 (s), 133.5 (d), 133.9 (d), 134.9 (s), 147.4 (s), 168.9 (s)
9a	2450 1670	217 (M^+) 183 (M^+-34)	1.60 (1H, s, SH), 2.95 (2H, m), 3.85, 4.65 (2H, m), 5.85 (2H, m, vinyl protons), 7.3—7.9 (4H, m, aromatic protons)	36.6 (t), 38.2 (t), 77.1 (s), 121.1 (d), 121.4 (d), 123.0 (d), 123.4 (d), 127.7 (s), 128.5 (d), 131.2 (d), 149.2 (s), 164.0 (s)
9b	2450 1690	231 (M^+) 197 (M^+-34)	1.15 (1H, s, SH), 2.75 (3H, s), 2.40, 2.80 (2H, m), 3.80, 4.45 (2H, m), 5.55 (1H, m, vinyl proton), 7.2—7.8 (aromatic protons)	17.8 (q), 37.1 (t), 38.9 (t), 71.2 (s), 122.4 (d), 123.0 (d), 124.1 (d), 128.7 (d), 129.5 (s), 13.8 (s), 132.5 (d), 150.0 (s), 163.8 (s)
9c-i	2450 1690	231 (M^+) 197 (M^+-34)	1.40 (3H, d, J=6 Hz), 2.10 (1H, s, SH), 2.35 (1H, m), 2.80, 3.60 (2H, m), 5.40, 5.80 (2H, m, vinyl protons), 7.2—7.8 (aromatic protons)	17.3 (q), 37.2 (t), 41.1 (d), 70.4 (s), 122.9 (d), 123.6 (d), 123.8 (d), 129.0 (d), 129.2 (d), 130.7 (s), 131.8 (d), 149.0 (s), 164.5 (s)
9c-ii	2450 1690	231 (M^+) 197 (M^+-34)	0.50 (3H, d, J=6 Hz), 2.65 (1H, s, SH), 3.00 (1H, m), 2.85, 3.60 (2H, m), 5.80 (2H, m, vinyl protons), 7.2—7.8 (aromatic protons)	17.2 (q), 37.5 (t), 41.6 (d), 69.7 (s), 122.7 (d), 123.0 (d), 123.8 (d), 128.8 (d), 129.0 (d), 131.2 (s), 132.0 (d), 147.9 (s), 165.6 (s)
9d	2450 1690	245 (M^+) 211 (M^+-34)	0.70 (3H, s), 1.40 (3H, s), 2.39 (1H, s, SH), 2.80, 3.55 (2H, m), 5.80 (2H, m, vinyl protons), 7.2—7.7 (4H, m, aromatic protons)	17.1 (q), 18.5 (q), 41.6 (t), 44.4 (s), 69.1 (s), 123.0 (d), 123.1 (d), 123.9 (d), 127.9 (d), 129.3 (d), 131.0 (s), 132.5 (d), 146.8 (s), 165.5 (s)

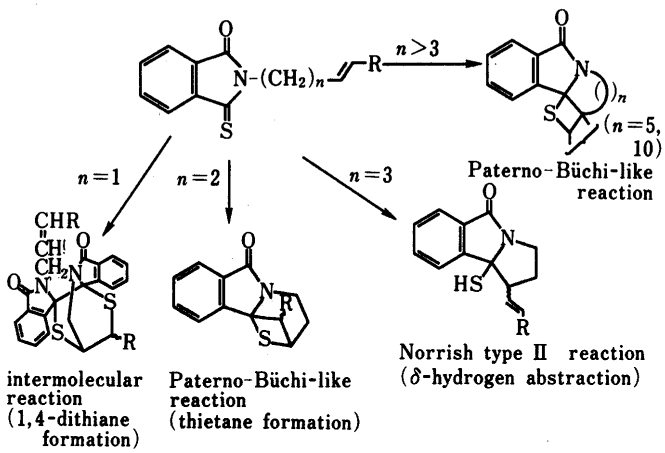

Chart 3

described above. As expected, the thietane **8e** (24%) was obtained accompanied with the pyridoisoindolone **9e** (14%).

Consequently, the reaction similar to that reported by Coyle and Rapley would proceed *via* pathway B, three stepwise processes (**4**→**5**→**6**) involving biradical intermediate (**4**) formation, thietane (**5**) formation, and subsequent cleavage of the thietane ring leading to the final products (**6**), but not *via* pathway A involving γ-hydrogen abstraction as outlined in Chart 1. From the above results, coupled with those reported in previous papers,[3-5] the overall photochemical behavior of the aromatic thioimide system has become apparent. As shown in Chart 3, when $n=1$ the initially generated biradical intermediate preferentially traps a second molecule of thioimide intermolecularly to form 1,4-dithianes.[7] In the case of $n=2$ the thioimide system is inert to the γ-hydrogen abstraction, which is a well-defined reaction in the imide.[8] By contrast, in the cases of $n \geqq 3$, the Norrish type II and Paterno–Büchi-like pathways are competitive, depending on the number of methylenes in the alkyl side chain.[5]

Experimental

All melting points were determined on a Yamato melting point apparatus (model MP-21) and are uncorrected. Infrared (IR) spectra were recorded on a JASCO A-102 spectrometer. Nuclear magnetic resonance (NMR) spectra were taken on a JEOL JNM FX-90Q spectrometer. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane (0.0 ppm) as an internal standard. The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; m, multiplet. Gas chromatography was performed with Hitachi 163 gas chromatograph (column: Fluoxylate-K). Mass spectra were obtained on a JEOL JMS-QH-100 gas chromatograph-mass spectrometer. Preparative irradiations were conducted by using a 1 kW high-pressure mercury lamp (Eikosha EHB-W-1000) through a Pyrex filter at room temperature. Stirring of the reaction mixture was effected by the introduction of a stream of nitrogen at the bottom of the outer jacket. Column chromatography was conducted using silica gel (Merck, Kieselgel 60, 70—230 mesh).

TABLE IV. Thioimides **7**

Thioimide	Yield (%)	Appearance	Formula	Analysis (%) Calcd (Found)			
				C	H	N	S
7a	41	Red oil	$C_{12}H_{11}NOS$	66.35	5.10	6.45	14.73
				(66.44	5.01	6.58	14.99)
7b	37	Red oil	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84
				(67.79	5.88	6.31	13.59)
7c	46	Red oil	$C_{13}H_{13}NOS$	67.52	5.67	6.06	13.84
				(67.48	5.55	6.18	13.95)
7d	38	Red oil	$C_{14}H_{15}NOS$	68.55	6.16	5.71	13.05
				(68.71	6.30	5.57	13.23)
7e[6]	34	Red oil					

Preparation of *N*-Substituted Thioimide Derivatives (1). General Procedure Imide derivatives were prepared by the reported procedure.[9] Thioimides (**7a—d**) were prepared from the corresponding imides and Lawesson's reagent according to the procedure described in ref. 3*a*, and purified by column chromatography (Table IV).

Irradiation of 7. General Procedure A solution of **7** (5 mmol) in benzene (500 ml) was irradiated for 1 h with a 1 kW high-pressure mercury lamp through a Pyrex filter under N_2 at room temperature or 0 °C. After removal of the solvent *in vacuo*, the residue was chromatographed over silica gel. The results are listed in Table I.

Irradiation of 8. General Procedure (Photochemical Conversion of 8 to 9) A solution of **8** (20 mg) in benzene (10 ml) was irradiated for 1 h with a 1 kW high-pressure mercury lamp through a Pyrex filter under an N_2 atmosphere. Product analyses were performed by gas chromatography.

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