

INTERMOLECULAR PHOTOADDITION OF N-METHYLPHthalIMIDE TO INDOLE DERIVATIVES:  
REGIO- AND STEREOSELECTIVE FORMATION OF OXETO[2,3-b]INDOLES<sup>1</sup>

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**Abstract** — N-Methylphthalimide in the presence of N-acylindole derivatives underwent a photochemical [2+2]cycloaddition to give more sterically hindered oxetanes in moderate yields. Some reactions of these imide-oxetanes are also described.

Phthalimides undergo a variety of photoreactions with alkenes<sup>2</sup>, including addition to the C(O)N bond, electron transfer, photoreduction and, only in few cases, imide-oxetane formation. During the course of systematic studies on imide photochemistry, we have found the first example of the oxetane formation of this aromatic imide system by intramolecular photolysis of N-( $\omega$ -indol-3-ylalkyl)phthalimides<sup>2e</sup>. To explore this reaction more extensively, we now have examined further the intermolecular photocycloaddition of N-methylphthalimide 1 with a series of N-acylindole derivatives 2, a good Paterno-Büchi acceptor<sup>2e,3</sup>.

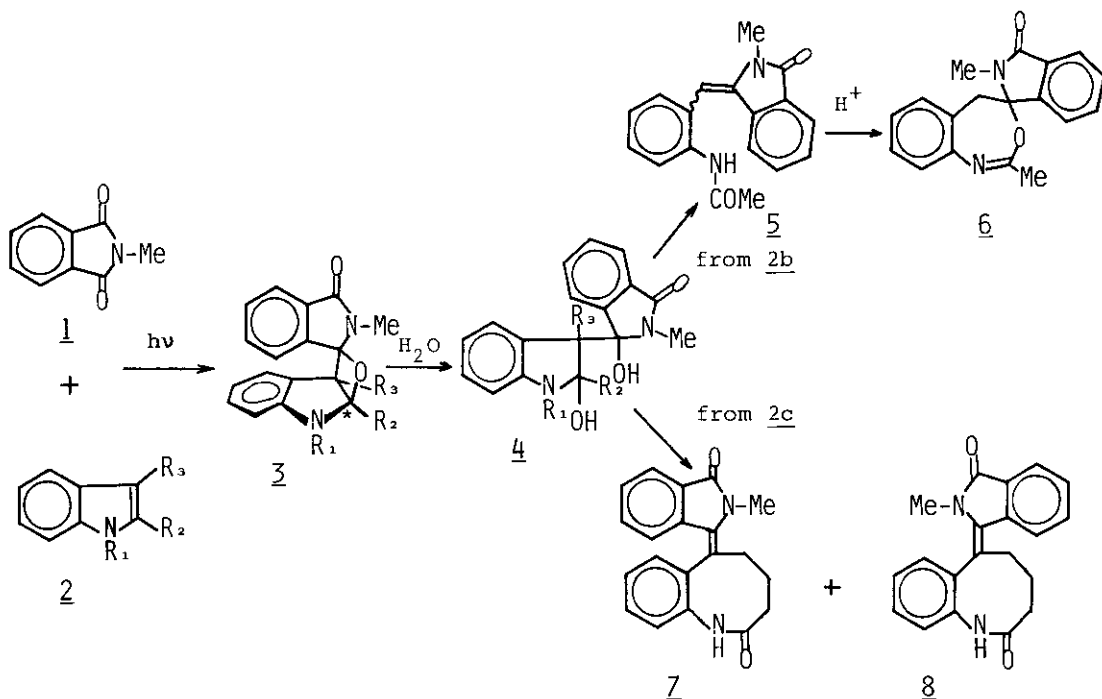
A solution of 1 and 2 (mole ratio 1:1) in acetone (10 mM) was irradiated under a nitrogen atmosphere with a Pyrex-filtered 500W high-pressure mercury lamp. As listed in Table I<sup>4</sup>, compounds 2a,d,e,f underwent [2+2]cycloaddition to give oxetanes 3a,d,e,f, respectively, after alumina column chromatography. In place of oxetane (3), compound 2b gave an enamide 5 and a spiro oxazepine derivative 6, while 2c afforded ring expanding products 7 and 8. These products 5-8 probably arised from the initially formed imide-oxetanes by hydrolysis followed by subsequent ring opening of the indoline ring (Scheme 1)<sup>2e</sup>.

The structures of photoproducts were assigned on the basis of microanalytical results and spectroscopic properties<sup>4</sup>. For example, in the <sup>1</sup>H-NMR spectrum of 3a

a methine\* proton on the oxetane ring showed a signal at 6.40 ppm, the chemical shift value of which is close to that of the methine proton adjacent to the nitrogen and oxygen atoms in the previously reported oxeto[2,3-b]indole system<sup>2e,5</sup>. In the <sup>13</sup>C-NMR spectra of oxetanes 3a,d,e,f, signals of a methine (in 3a) and a quaternary (in 3d,e,f) carbon\* appeared at 94.5-100 ppm, and those of other two quaternary carbons on the oxetane ring appeared at 59.5-66.3 ppm and 102.7-103.6 ppm, respectively, suggesting that regioselective [2+2]cycloaddition reaction of 1 and 2 has occurred. Furthermore, in 3a,d,e,f, two protons of aromatic ring showed a pronounced shielding effect (5.95-6.60 ppm), indicating the stereochemical structure 3 as illustrated in Scheme 1.

It is noteworthy that this reaction afforded exclusively the more sterically hindered oxetane 3 as a single stereoisomer, in which the aromatic rings of the isoindolone and the indoline moiety overlap each other. Such a hindered oxetane formation was also observed in the naphthalic anhydride-indene system, resulting from the excited complex that has the same configuration with  $\pi$ -overlapping as the ground state complex<sup>6</sup>. These results would suggest a possible involvement of certain stacking interaction, such as an excited complex, between the aromatic rings of phthalimide 1 (a good electron acceptor)<sup>7</sup> and indole derivatives 2, although none of the spectroscopic evidence is so far obtained. In parallel to this inference, when the N-acyl group in 2 is a electron-attractive methoxycarbonyl group (2f) the yield of 3 decreased, and no oxetane was obtained when N-trifluoroacetyltetrahydrocarbazole was used.

The intermolecular photocycloaddition reactions of the imides and various Paterno-Büchi acceptors (oxetane-forming partners), as illustrated in the present example, would lead to interesting transformations by way of the intermediate imide-oxetane. The detailed mechanism of this reaction is under investigation.



Scheme 1

 Table I Photoproducts from the Reaction of 1 with 2

<u>2</u>	Substrate			Time (h)	Product	Yield (%)	mp °C	Recovery of <u>1</u> (%) and <u>2</u> (%)	
	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>						
<u>a</u>	COMe	H	Me	2	<u>3a</u>	18	196-198	73	56
<u>b**</u>	COMe	Me	H	2	<u>5</u>	16	265-266.5	25	14
					<u>6</u>	32	123.5-124.5		
<u>c</u>	COMe	-(CH <sub>2</sub> ) <sub>3</sub> -		3	<u>7</u>	41	273.5-275.5	34	11
					<u>8</u>	6	286-287		
<u>d</u>	COMe	-(CH <sub>2</sub> ) <sub>4</sub> -		2	<u>3d</u>	62	184-186	20	14
<u>e</u>	COMe	-(CH <sub>2</sub> ) <sub>5</sub> -		2	<u>3e</u>	39	201-205	54	22
<u>f</u>	CO <sub>2</sub> Me	-(CH <sub>2</sub> ) <sub>4</sub> -		4	<u>3f</u>	34	185-187.5	19	21

\*\* After irradiation the photolysate was treated with TsOH.

REFERENCES AND NOTES

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- 4) All new compounds gave satisfactory elemental analyses, and their structures were supported by spectral (IR, <sup>1</sup>H-NMR, <sup>13</sup>C-NMR, MS) data. Compound 5: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 6.50 (1H, s, CH=C); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ: 165.2(s), 168.3(s) (CO-N×2). Compound 6: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.38 and 3.72 (2H, ABq, J=17.7 Hz, -CH<sub>2</sub>-); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ: 42.0 (t, -CH<sub>2</sub>-), 84.0 (s, O-C-N-CH<sub>3</sub>), 166.3(s), 169.8(s) (amide carbon and oxazepine carbon). Compound 7: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 3.60 (3H, s, N-CH<sub>3</sub>); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ: 26.4(t), 32.9(t), 34.0(t) (-(CH<sub>2</sub>)<sub>3</sub>-), 168.0(s), 175.6(s) (CO-N×2). Compound 8: <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 2.47 (3H, s, N-CH<sub>3</sub>); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ: 23.6(t), 33.5(t), 35.7(t) (-(CH<sub>2</sub>)<sub>3</sub>-), 167.8(s), 176.2(s) (CO-N×2).
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