INTERMOLECULAR PHOTOADDITION OF N-METHYLPHTHALIMIDE TO INDOLE DERIVATIVES: REGIO- AND STEREOSELECTIVE FORMATION OF OXETO[2,3-b]INDOLES[1]

Haruko Takechi* and Minoru Machida
Faculty of Pharmaceutical Sciences, Higashi-Nippon-Gakuen University,
Ishikari-Tobetsu, Hokkaido, 061-02 Japan
Yuichi Kanaoka*
Faculty of Pharmaceutical Sciences, Hokkaido University,
Sapporo 060, Japan

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[2], 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-(ω-indol-3-ylalkyl)phthalimides[2e]. 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[2e,3].

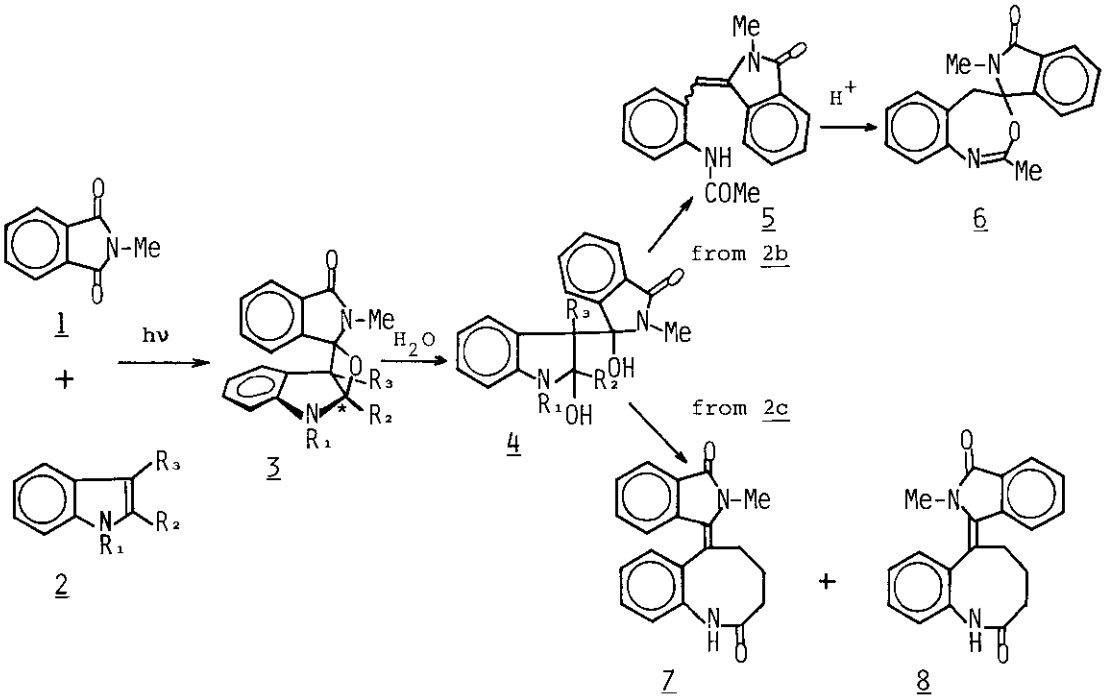
A solution of 1 and 2 (mole ratio 1:1) in acetone (10 mM) was irradiated under a nitrogen atmosphere with a Pyrex-filtered 500W high-pressure mercury lamp. As listed in Table I[4], compounds 2a,d,e,f underwent [2+2]cycloaddition to give oxetanes 3a,d,e,f, respectively, after alumina column chromatography. 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)[2e].

The structures of photoproducts were assigned on the basis of microanalytical results and spectroscopic properties[4]. For example, in the ^{1}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[2e,5]. In the ^{13}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 π-overlapping as the ground state complex[6]. 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)[7] 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

2	Substrate R_1	R_2	R_3	Time (h)	Product	Yield (%)	mp °C	Recovery of 1(%)	and 2(%)
a	COMe	H	Me	2	3a	18	196-198	73	56
b**	COMe	Me	H	2	5	16	265-266.5	25	14
					6	32	123.5-124.5		
c	COMe	$-(CH_2)_3-$		3	7	41	273.5-275.5	34	11
					8	6	286-287		
d	COMe	$-(CH_2)_4-$		2	3d	62	184-186	20	14
e	COMe	$-(CH_2)_5-$		2	3e	39	201-205	54	22
f	CO_2Me	$-(CH_2)_4-$		4	3f	34	185-187.5	19	21

** After irradiation the photolysate was treated with TsOH.

REFERENCES AND NOTES

1) a) Photochemistry of the Phthalimide System. 38. Part 37: Y. Sato, H. Nakai, M. Wada, T. Mizoguchi, Y. Hatanaka, Y. Migita, and Y. Kanaoka, submitted;
b) Photoinduced Reactions. 75. Part 74: E. Sato and Y.Kanaoka, Chem. Pharm. Bull., 33, in press.

2) a) P. H. Mazzocchi, "Organic Photochemistry", Vol. 5, A. Padwa, Ed., Marcel Dekker, Inc., New York, 1981, p 421;
b) P. H. Mazzocchi, S. Minamikawa, P. Wilson, M. Bowen, and N. Narian, J. Org. Chem., 1981, 46, 4846;
c) K. Maruyama and Y. Kubo, J. Org. Chem., 1981, 46, 3612;
d) M. Machida, K. Oda, and Y. Kanaoka, Chem. Pharm. Bull., 1984, 32, 75 and references cited therein;
e) M. Machida, H. Takechi, and Y. Kanaoka, Tetrahedron Letters, 1982, 23, 4981.

3) P. H. Mazzocchi, L. Klingler, M. Edwards, P. Wilson, and D. Shook, Tetrahedron Letters, 1983, 24, 143.

4) All new compounds gave satisfactory elemental analyses, and their structures were supported by spectral (IR, ^{1}H-NMR, ^{13}C-NMR, MS) data. Compound 5: ^{1}H-NMR ($CDCl_3$) δ: 6.50 (1H, s, CH=C); ^{13}C-NMR ($CDCl_3$) δ: 165.2(s), 168.3(s) (CO-N×2). Compound 6: ^{1}H-NMR ($CDCl_3$) δ: 3.38 and 3.72 (2H, ABq, J=17.7 Hz, $-CH_2-$); ^{13}C-NMR ($CDCl_3$) δ: 42.0 (t, $-CH_2-$), 84.0 (s, O-C-N-CH_3), 166.3(s), 169.8(s) (amide carbon and oxazepine carbon). Compound 7: ^{1}H-NMR ($CDCl_3$) δ: 3.60 (3H, s, N-CH_3); ^{13}C-NMR ($CDCl_3$) δ: 26.4(t), 32.9(t), 34.0(t) ($-(CH_2)_3-$), 168.0(s), 175.6(s) (CO-N×2). Compound 8: ^{1}H-NMR ($CDCl_3$) δ: 2.47 (3H, s, N-CH_3); ^{13}C-NMR ($CDCl_3$) δ: 23.6(t), 33.5(t), 35.7(t) ($-(CH_2)_3-$), 167.8(s), 176.2(s) (CO-N×2).

5) D. R. Julian and G. D. Tringham, J. Chem. Soc. Chem. Comm., 1973, 13.

6) S. Farid and S. E. Shealer, J. Chem. Soc. Chem. Comm., 1973, 296.

7) Y. Kanaoka, Accounts Chem. Res., 1978, 11, 407.

Received, 19th February, 1985