PHOTOCYCLIZATION OF N-3-ALKENYLPHTHALIMIDES.[1]
EFFECT OF ALKYL SUBSTITUTION ON THE FORMATION OF PYRROLOISOINDOLES AND PYRIDOISOINDOLES

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Abstract —— Photolysis of N-3-alkenylphthalimides 1 in methanol gave tetrahydro-5H-pyrrolo[2,1-a]isoindol-5-ones 2 and/or tetrahydropyrido[2,1-a]-isoindol-6(2H)-ones 3 depending on the degree of substitution at the olefin carbons of 1. Electron transfer followed by the anti-Markownikoff addition of methanol is proposed as a possible mechanistic pathway.

Recently there has been a great deal of interest in the photochemistry of cyclic imides,[3] which undergo a variety of photoreactions common to simple carbonyl compounds including inter- and intramolecular photoaddition of olefins.[4,5] We reported that N-alkenylphthalimides undergo photocyclization giving several 1,2,3,9b-tetrahydro-5H-pyrrolo[2,1-a]isoindol-5-one derivatives.[5a] During studies on the scope of these reactions, we investigated in the present work the photolysis of a set of N-3-alkenylphthalimides 1 with all combination of methyl substituents.

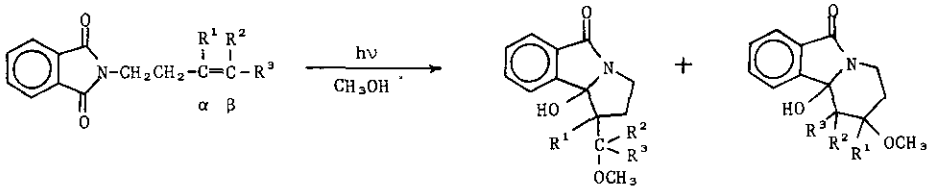
The N-3-alkenylphthalimides 1a-f were prepared in moderate yields by reacting potassium phthalimide with appropriate 1-halo-3-alkenes in dimethylformamide. In a representative example, irradiation of a solution of 1b in methanol (10 mM)[6] afforded, after silica gel chromatography (chloroform : ethyl acetate = 8 : 1), two diastereoisomers ($C_{14}H_{17}NO_3$) 2b-i and 2b-ii in a good total yield. Compound 2b-i showed : IR (KBr) 3230 (OH), 1670 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ: 0.50 (3H, s, C-Me), 1.7-2.1 (2H, m, N-CH_2<u>CH_2</u>), 2.2-2.7 (2H, m, <u>CH_2</u>OMe), 3.2-3.8 (2H, m, N-CH_2), 3.50 (3H, s, OMe), 4.10 (1H, s, OH), 7.3-7.7 (4H, m, aromatic H). Compound 2b-ii showed : IR (KBr) 3350 (OH), 1690 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ : 1.30 (3H, s, C-Me). The stereochemistry of 2b-i was assigned as shown in Chart I on the basis of their ^{1}H NMR spectra by considering the anisotropic shielding effects of the phenyl ring on the chemical shifts of the C-methyl, namely, C-Me (2b-ii − 2b-i) = 0.8 ppm.


2b-i

2b-ii

Chart I

Similarly, irradiation was carried out on the N-3-alkenylphthalimides (1a,1c-f), and the results were summarized in Table I. Similar results as in the case of 1b were observed on the compounds (1a *and* 1d), *thus forming* only a stereomixture of the pyrroloisoindolones (2), while the pyridoisoindolone (3) was the sole product from 1e. However, the reaction of 1c and 1f afforded a mixture of 2 and 3 (Scheme I).


1

2

3

Scheme I

Table I. Photolysis of 1 and the Product Distribution

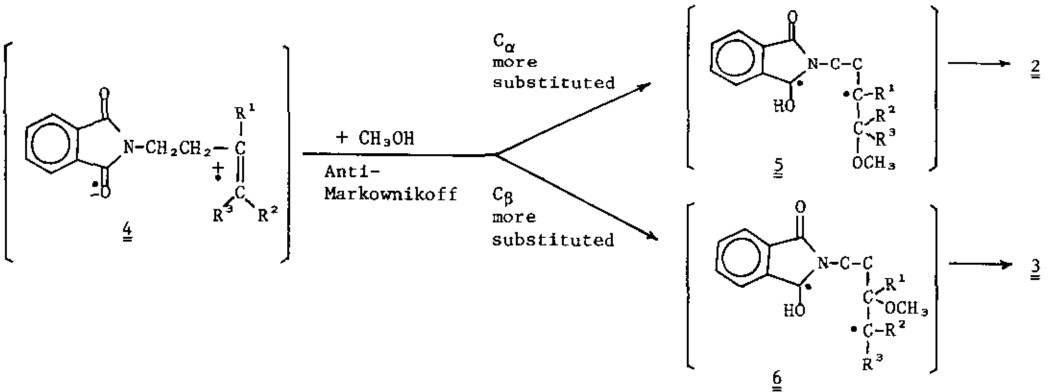
1	R^1	R^2	R^3	2 Yield (%) (mp. °C)		3 Yield (%) (mp. °C)	
a	H	H	H	9[1*] (150-152)			
b	CH_3	H	H	i 52 (156-158.5)	ii 31 (162-163)		
c	H	CH_3	H	i 18 (164.5-165.5)	ii 14 (168.5-170)	39 (161-163.5)	
d	CH_3	CH_3	H	i 17 (168-170.5) iii 19 (159-162)	ii 27 (177-179)		
e[2*]	H	CH_3	CH_3			i 42 (198-200)	ii 41 (111-112)
f[3*]	CH_3	CH_3	CH_3	11 (99.5-101)		i 9 (117-119)	ii 18 (154-156)

[1*] 61 % of 1a was recovered.

[2*] cf. Ref. 5a

[3*] An unknown product (mp. 108-110°C) was also formed.

It is interesting that such rather little variation in the substrate structures as the existence of a methyl group has profoundly influenced the reaction sites mostly resulting in predominant formation of either the pyrroloisoindolones 2 or pyridoisoindolones 3. The photoproducts consist of a mixture of stereoisomers which were separated by silica gel chromatography, and most of their structures were assigned based on the analyses of their ^{1}H NMR spectra as in the case of 2b. Mazzocchi *et al*. extensively studied the intermolecular photochemical addition of dienes[7a] and olefins[7b-d] to N-methylphthalimide, and have shown that the remarkable sensitivity of the addition process to alkene ionization potential is due to competitive electron transfer quenching of the phthalimide excited state by the alkene.[7c] Analogous results have been found by Maruyama *et al*.[5] Although the mechanism of the reaction is still open to question, the gross features may include such initial electron transfer at least as one of the important processes. The results in the Table which were obtained with the intramolecular addition may also be best rationalized by considering such pathways. Thus the electron transfer from the double bond in the side chain to the imide is followed by the anti-Markownikoff addition of methanol,[5a,8] forming a more stabilized biradical intermediate among two possible ones. With the substrates in which the C_α atom is more substituted the biradical (5) would be formed and then give rise to the product 2(a,b,d), while with that having the C_β atom more substituted the biradical is 6 leading to 3(e) (Scheme II). When the C_α and C_β atoms are substituted to the equal extent as in the case of c and f, both products indeed were formed. The above formulation provides reasonable interpretation in all cases for the product distribution.



Scheme II

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