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PHOTOCYCLIZATION OF N-ARALKYLPHTHALIMIDES: AN EXAMPLE OF POSSIBLE SYNTHETIC CONTROL IN A HETEROCYCLIC SERIES[1,2]

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Photocyclization of various N-alkylphthalimides has been the subject of recent work[3]. It has been shown that the general pattern involves Norrish type II reactions including the γ- and δ-hydrogen transfers presumably by way of biradical intermediates[3a]. We now wish to report the results of the photolysis of N-ω-arylalkylphthalimides 1 which are of interest because the cyclization exhibits pronounced dependency on the aromatic substituents and the side-chain length.

Irradiation of 1 (n=2,3; X = H) failed to yield 2 (n=2,3; X = H) giving complex mixtures of minor products. Therefore, it was rather unexpected when 1 (n=4; X = H) gave the cyclized product 2 (n=4; X = H), though in a poor yield, because 2 (n=2,3,4) are apparently the γ-, δ- and ε-hydrogen transfer products in the Norrish type II reaction, respectively, and the reactivity order γ > δ ≫ ε in such a reaction has been well documented[4]. Moreover, 1 (n=4; X = *o*-, *m*-, *p*-Me) gave the same ring system 2 (n=4; X = *o*-, *m*-, *p*-Me) in distinctly better yields. The inference that electron-donating substituents on the benzene ring promote the cyclization was further supported by the fact that 2 (n=4; X = m,p-diMe) was similarly obtained in 47% yields. As expected, methoxy groups showed the same or better effect on this reaction to afford 2 (n=4; X = *o*-, *m*-, *m*,*p*-diMeO). This promoting effect of an electron-donating substituent was successfully applied to synthesize the homologous members of a smaller ring size, 2 (n=3; X = *o*-, *p*-, *m*,*p*-diMeO), though the yields were lower than those in 2 (n=4). While 1 (n=5; X = *p*-MeO) was converted into 2 (n=5; X = *p*-MeO), 1 (n=6; X = *m*,*p*-diMeO) failed to cyclize indicative of the optimum ring size, i.e. n=4, in this particular reaction. These results are listed in the Table I.[5]

The favored status of reactions with six- as compared to seven- or more-membered cyclic transition states, in general, has been established[6] in chemical literature including recent photoreactions[4,7]. It is, therefore, remarkable that in the above-mentioned examples the cyclization occurs best to give 2 (n=4) thus reflecting a marked facility for the ε-hydrogen transfer (presumably 1, 8-hydrogen abstraction-cyclization) which indicates preference for usually unfavorable eight-membered transition states (3; n=4) relative to those of seven- and six-membered (3; n=3,2). Thus a special mechanism must be involved which may be associated with some interaction between the imide carbonyl and the benzylic methylene.

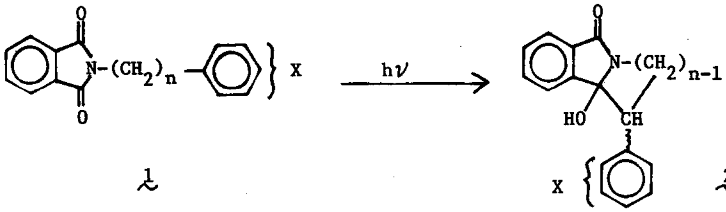
In view of that the phthalimide system is capable of forming a charge-transfer complex with electron donors[8], it seems reasonable to assume that the cyclization is a result of enhanced hydrogen abstraction from the benzylic methylene which is held in close proximity to the excited imide carbonyl through postulated complex formation 4.[9] The methylene chain-length permitting effective interaction of the two chromophores[8b] apparently ranges within n=3~5 in this case. In addition, the substituents on the benzene ring may also affect the distribution between extended, unreactive conformers and coiled, reactive conformers.

In general, combination of donor-acceptor pairs, varying in the stability of the complex and geometry of the arrangement of the components, provides good models for "synthetic control" of the photocyclization, which may represent a useful approach to specificity in synthetic chemistry.[10] We are presently investigating the generalization of such a "photolysis of donor-acceptor pair" system with possible hyperentropic effects.[11]

Table I Yields (%) of the photo-products 2

n	X = H	o-Me	m-Me	p-Me	m,p-Me_2	o-MeO	p-MeO	m,p-$(MeO)_2$
3 (δ)	~0					16 (164.5-66)	12 (154-5.5)	21 (180-2)
4 (ε)	4* (172-3.5)	11 (181-2.5)	22 (178.5-80)	42 (158-60)	46 (172-4)	25 (181-4)	47 (159-61.5)	30 (156-8)
5 (ζ)						~0	11 (193-5)	
6								~0

* 5hr. Mp (in most cases melting with bubbling) are shown in parenthesis.



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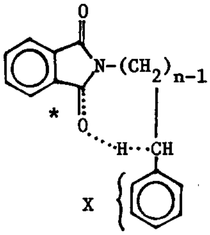

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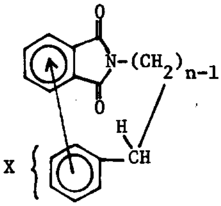

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(9) No direct intramolecular interaction between the phthalimide and aromatic moieties of **1** as monitored by uv absorption have been detected so far. However, a weak charge-transfer band is observed in the uv spectrum of an ethanol solution of N-methylphthalimide (3mM) containing anisole (1.0M) to indicate the existence of intermolecular interaction between the two moieties in the ground-states. Furthermore, it was found that fluorescence of anisole (ex. 280 nm, em.maximum 310 nm, 1.0M in ethanol) is quenched in presence of N-methylphthalimide ($10^{-1} \sim 10^{-2}$mM). These results suggest that intramolecular interaction of the two chromophores of **1** either in the ground- or excited-states could well operate to form a complex thus freezing degree of freedom at the transition states.

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