Tetrahedron Letters No. 14, pp 1193 - 1196, 1973. Pergamon Press. Printed in Great Britain.

PHOTOCHEMISTRY OF THE PHTHALIMIDE SYSTEM. IV*. PHOTOCYCLIZATION OF N-ALKYLPHTHALIMIDES TO BENZAZEPINONE LACTAMS: UNUSUAL TWO-FOLD NORRISH TYPE II REACTIONS**

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(Received in Japan 9 February 1973; received in UK for publication 27 February 1973)

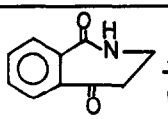
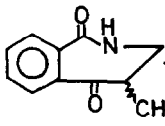
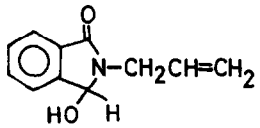
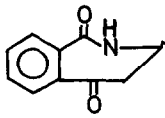
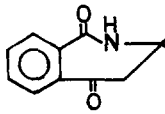
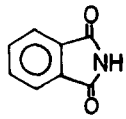
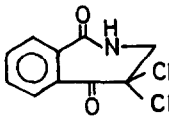
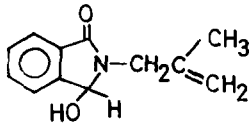
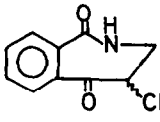
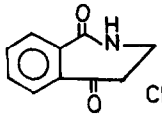
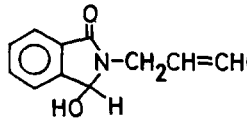
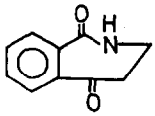
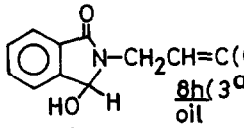
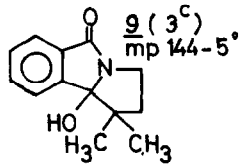
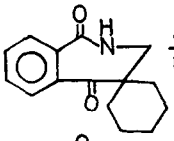
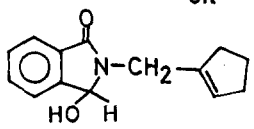
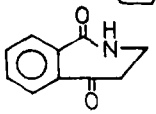
Certain suitably substituted phthalimides undergo photocyclization to afford corresponding aza-cyclopentanol derivatives as a result of relatively facile δ-hydrogen abstraction (1,2). In view of intense activity in the photochemistry of carbonyl compounds (3), studies are undertaken to provide further information about the nature of the photochemical behaviors of the phthalimide system. We wish to present here the general pattern of the photolysis of N-alkylphthalimides.

A series of N-alkylphthalimides $\underline{1a} \sim \underline{1}$, which have γ-(and δ-)hydrogens and none of heteroatoms in the side chains (4), were synthetized and their photolysis was examined. Assigned structures of the photoproducts and their isolation yields are listed in Table I (5). The most striking result is that nearly all the phthalimides afford benzazepinone lactams $\underline{4}$,$\underline{6}$ as the common products. In addition, in several cases the dihydrophthalimides with an unsaturated alkyl group $\underline{8}$ were obtained. From $\underline{1h}$, small amount of $\underline{9}$ was isolated together with $\underline{6}$ and $\underline{8h}$.

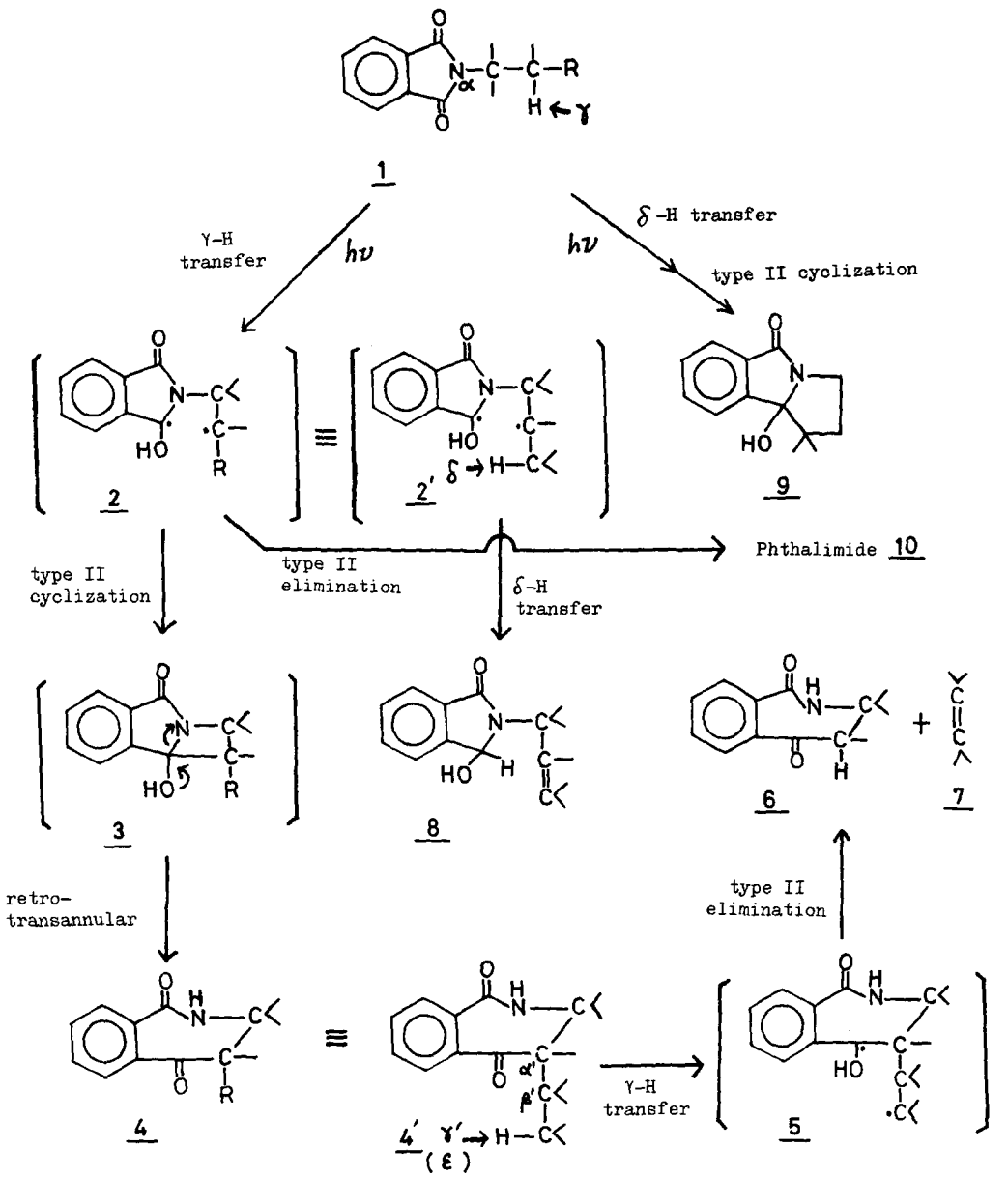
These results may be best rationalized by considering the proposed scheme on the basis of strictly formal analogy with the Norrish type II mechanism established in the simple ketone system (3). The substrate $\underline{1}$ undergoes initial γ-hydrogen abstraction to form a biradical intermediate $\underline{2}$, followed by the type II cyclization to an aza-cyclobutanol $\underline{3}$ which, presumably due to its strained structure, through a subsequent retro-transannular ring opening leads to the benz-

* For Part III see ref. (1). ** Photoinduced Reactions. X.

Table I Photoproducts from N-Alkylphthalimides

Alkyl	4, 6	8	9, 10
$-CH_2CH_3$ 1a	 4a(6[a], 3[b]) mp 161-3°		
$-CH_2CH_2CH_3$ 1b	 4b(39[a], 29[b]) mp 160-1°	 8b(18[a]) oil	
$-CH(CH_3)_2$ 1c	 4c(5[a], 2[b]) mp 227-8°		
$-C(CH_3)_3$ 1d	 4d(20[b],4[c]) mp 159-60°		 10 (10[b])
$-CH_2CH(CH_3)_2$ 1e	 4e(8[c]) mp 183-5°	 8e(10[c]) mp 86-7°	
$-CH_2CH(CH_3)(C_2H_5)$ 1f	 6 ≡ 4b (14[a])		
$-CH_2CH_2CH_2CH_3$ 1g	 6≡4a(18[a],14[b]) $CH_2=CH_2$ 7(4[a])	 8g (17[a]) oil	
$-CH_2CH_2CH(CH_3)_2$ 1h	 6≡4a(23[a],5[c])	 8h(3[a]) oil	 9 (3[c]) mp 144-5°
$-CH_2$-Cycl 1i,j	 4j(1[a]) mp 169-71°	 8i(19[a]) mp 104-5°	
$-CH_2CH_2$-Cycl 1k,l	 6≡4a (16~21[a])		

solvent: a, acetonitrile; b, t-butanol; c, acetone. Cycl: cyclopentyl (i,k) and cyclohexyl (j,l). % isolation yields shown in parenthesis; no corrections were made based on the recovered substrates. Irradition time, 1-14hr.



azepinone lactam 4. Alternatively, in some of the biradicals with δ-hydrogen 2', competing δ-hydrogen transfer takes place to concomitant formation of the unsaturated dihydro product 8. When the initial product 4' has still a γ-hydrogen that is ε in the original substrate, the second

γ-hydrogen abstraction now follows and, the type II elimination, again by way of the biradical 5, ultimately affords the benzazepinone lactam 6 accompanied by an olefine fragment 7. With a substrate 1 having a δ-hydrogen another type II cyclization may afford an aza-cyclopentanol derivative 9.

Although it is possible that some products are missing by technical difficulty in the course of working-up, the above formulation provides reasonable interpretation in most cases for the product distributions in Table I. Compounds 1a, 1c, and 1d, which lack δ-hydrogen gave the corresponding lactams 4a, 4c, and 4d, respectively, as normal type II cyclization products 4 in low yields. Formation of 4d seems favored by a statistical factor, while 10 may be the product of the type II elimination. The nature of γ-hydrogen which varies from primary to secondary to tertiary, influences the γ-C-H bond strength and hence the reaction rate (3,6). Increased yields of the formation of 4b and 4e may reflect this effect of alkyl substituents at the γ-carbon. The occurrence of 8b, 8e, 8g, 8h and 8i to a significant extent from 1b, 1e, 1g, 1h and 1i, respectively, is remarkable in contrast to the minor reactivity of δ-hydrogen in usual ketone system (3,6), consistently indicating the important reactivity of δ-hydrogens in the phthalimide system (1,2). The common product 6≡4a from 1g, 1h, 1k and 1l arises most probably from the two-fold type II processes with the elimination as the second step. Whereas 4j is the first type II cyclization product 4 remaining survived, 6f is the end product 6 derived from the intermediate 4 by the cleavage of the ethyl group in preference to the methyl group that has no γ-hydrogens. Identification of ethylene as its dibromide 7g gave evidence which supports this scheme. Systematic studies of the photocyclization of phthalimides including the synthetic application designed on the basis of this proposed formulation are under way.

Acknowledgment Y.S., H.N. and T.M. are grateful to Mr. M.Yamazaki, Director, for encouragement.

References

(1) Y.Kanaoka, Y.Migita, Y.Sato and H.Nakai, Tetrahedron Letters, (1973) 51.
(2) Y.Kanaoka and K.Koyama, ibid., (1972) 4517.
(3) For example, see: P.J.Wagner, Accounts Chem. Res., 4, 168 (1971); papers cited in ref. (2).
(4) The N atom in the phthalimide system is regard as α with respect to the imide carbon (1,2).
(5) Photolyses were performed with a 1kW or 400W high pressure mercury lamp in acetonitrile, t-butanol or acetone as stated. Products were purified through preparative tlc or column chromatography (silica gel). All new compounds had reasonable spectral properties (uv, ir, nmr and mass), and showed satisfactory analytical results.
(6) P.J.Wagner, P.A.Kelso, A.E.Kemppainen and R.G.Zepp, J.Am.Chem.Soc., 94, 7500 (1972).