

PHOTOCHEMISTRY OF SUCCINIMIDES

WITH AN ETHER OR A THIOETHER IN THEIR SIDE-CHAINS.

 γ - AND δ - HYDROGEN ABSTRACTION¹

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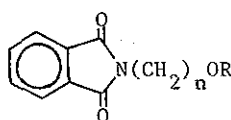
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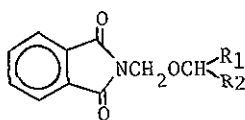
Upon irradiation certain N- β -sec-alkoxyalkyl-substituted succinimides 4 afforded a pyrrolo[1,2-c]oxazole ring system 5, δ -hydrogen transfer products, in moderate yields. On the other hand, the thioether analogs 11, 17 gave mixtures of γ -products (13, 14, 15, 18) and δ -products (16, 19), in low yields.

In 1972 we have found that N-substituted phthalimides, a parent system of aromatic cyclic imides, exhibit versatile and intriguing properties upon electron excitation,² and the observations were followed by systematic studies of the synthetic photochemistry of phthalimides.^{3,4} As a logical extension of the work, we were motivated to investigate the photochemistry of their aliphatic counterparts, alicyclic imides. Indeed, irradiation of a series of N-substituted alicyclic imides resulted in reactions arising from initial γ -hydrogen abstraction, i.e., type II cyclization and elimination.⁵ The former reaction, being rather dominant, led to syntheses of a variety

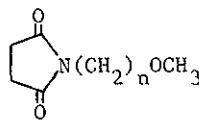
of ring-expanded products^{1,5} by way of retro-transannular ring opening of the intermediate cyclobutanols. In the subsequent studies of the aromatic series, we have proceeded to see photochemical behavior of phthalimides with an ether moiety in their N-side chains 1,⁶ which revealed the occurrence of photocyclization arising from δ -hydrogen abstraction, a work immediately followed by photochemical synthesis of a spiro ring system from 2 by using this technique.⁷ In a parallel work of the corresponding aliphatic series, the present paper describes photoreactions of succinimides with an ether or thioether moiety in their N-side chains in order to see the effect of the oxygen and the sulfur atoms on the photochemical behavior of the alicyclic imides.



1

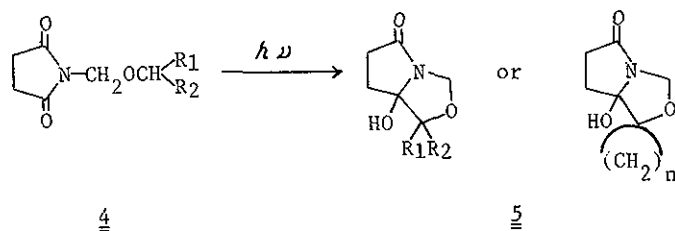


2



3

Independently to our work, Maruyama and Kubo reported that some of N- ω -methoxyalkylsuccinimides 3 undergo photocyclization due to δ -hydrogen abstraction ($n=1,3$).⁸ We have selected the compounds 4a-e, which lack γ -hydrogen and have a δ -carbon with a hydrogen and alkyl or methylene substituents (R_1-R_2), aliphatic analogs very similar to 2.⁷ A solution of 4 in acetonitrile (3-7mM) was irradiated with a 100-w low-pressure mercury lamp, and the products were purified by column chromatography (silica gel, CHCl_3 : AcOEt=1:1), and the results are listed in Table I.⁹ In all cases, the expected cyclized products 5 with a quaternary carbon, including spiro compounds with varying ring size (5-8 membered; 5b-e), were obtained in moderate isolated yields. In a typical example, the structural assignment for

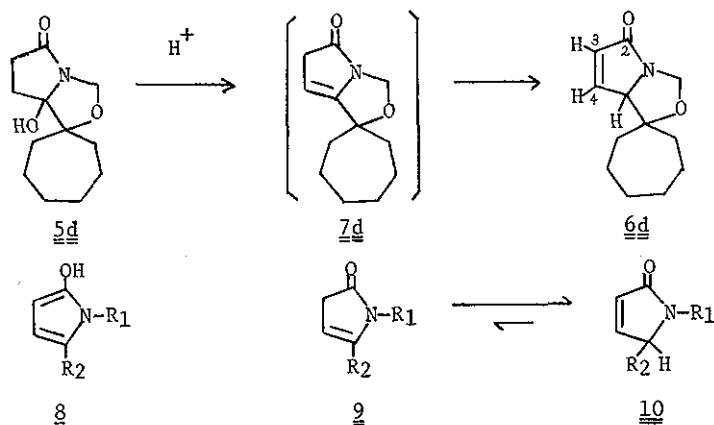
Table I Photoproducts from 4

<u>4</u>	$R_1 = R_2 \text{ or } R_1-R_2$	hr	<u>5</u> (%)	mp °c
<u>a</u>	Me	2.5	75	128-9
<u>b</u>	$-(CH_2)_4-$	2.0	45	122-3
<u>c</u>	$-(CH_2)_5-$	2.0	45	114-5
<u>d</u>	$-(CH_2)_6-$	1.2	68	121-2
<u>e</u>	$-(CH_2)_7-$	1.4	41	133-4

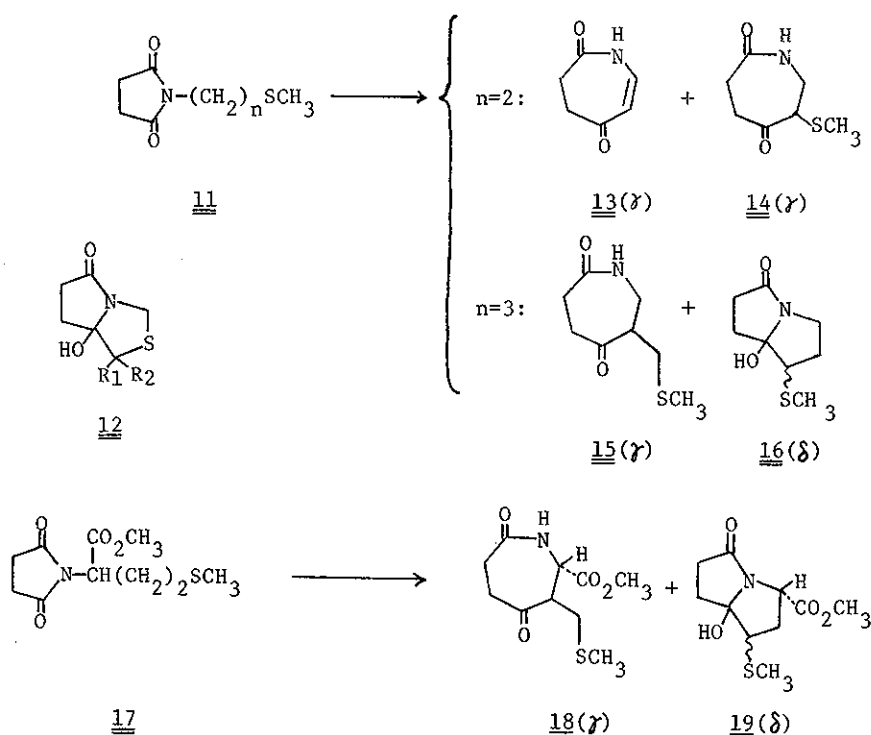
5a was based on (i) the presence of hydroxyl (ir 3275cm^{-1}) and an amide (1675cm^{-1}) in place of an imide; (ii) the absence of the methine in nmr; (iii) the molecular weight and composition, $C_8H_{13}NO_3$ (mass spectra and elemental analysis). These results now confirm that, also in the aliphatic series, the imide carbonyl undergoes type II cyclization via abstraction of δ -hydrogen which is activated by the adjacent oxygen,¹⁰ and that this reaction can be employed for photochemical synthesis of certain heterocyclic systems.

In order to see chemical properties of the resultant azaoxacyclopentanols 5, they were treated with acid and it was found that the hydroxyl group is readily dehydrated consistent with the assigned structures. For example, a solution of 5d in benzene was warmed in the presence of p-toluenesulfonic

acid for 20 min to give 6d (oil, 40 %). It is interesting to note that the product is not the Δ^4 -pyrrolin-2-one 7d but the Δ^3 -pyrroline-2-one derivative 6d, whose structure was established by its nmr spectrum [6.14ppm d,d, J=6 Hz, 2 Hz, (C_3 -H); 7.20, d,d, J=6,2(C_4 -H); 4.25,m, (C_5 -H)]. This conclusion is in agreement with the tautomeric nature of 2-hydroxypyrrole 8, which is known to exist in the form of 10 and not 9.¹¹



By contrast, the succinimides 11 with a thioether in their side chains showed markedly different photochemical behavior. The sulfur analogs 11 (n=1) of 4a, for example, resisted the reaction upon irradiation, failing to give the cyclized product 12, indicative of decreased photoreactivity of the hydrogen of the δ -carbon bonded to sulfur. However, photolysis of methylthio compound 11 (n=2), which has γ -carbon adjacent to sulfur, produced the seven-membered lactams 13 (mp 155-7°) and 14 (mp 122-3°), the γ -hydrogen transfer products, though only in 3 % yield each. The thioether 11 (n=3) possessing both the γ - and δ -hydrogens exhibited rather comparable reactivities giving rise to the γ - 15 (mp 99-100°; 5 %) and the δ -product 16 (mp 100-2°; 5 %). As an example of the synthetic application, photolysis of N-succinyl-L-methionine methyl ester 17 was performed. The expected γ -pro-



duct 18 (mp 156-7°; 9 %) and δ -products 19 (mp 113-25°; 7 %) were obtained.

There are two parallel lines of research problems to be solved in the photochemistry of cyclic imides; *i.e.*, aromatic and aliphatic. One major distinction between aromatic and aliphatic cyclic imides is in that the aromatic imide system can be a good electron acceptor,¹² which could favorably interact with a donor molecule such as thioether, either inter- or intra-molecularly, in the course of photoreactions. In agreement with the notion, a remarkable "cyclizing ability" of alkylthio-containing phthalimides was recognized and utilized for a synthesis of macrocycles.^{4,12} Since aliphatic cyclic imides without a benzene ring have no sufficient capacity as an acceptor, the thioethers 11 no longer exhibit such unusual

photoreactivities. Comprehensive photochemical studies of these two classes of imides are still under way in our laboratories.

ACKNOWLEDGEMENTS We would like to express our gratitude to Professor Shigehiko Sugasawa, on the occasion of his 80th birthday, for his continuous guidance and encouragement.

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Received, 5th August, 1977