PHOTOREACTIONS IN THE SYNTHESIS OF HETEROCYCLES. DESIGNS WITH AMIDES AND IMIDES AS SYNTHON CHROMOPHORES

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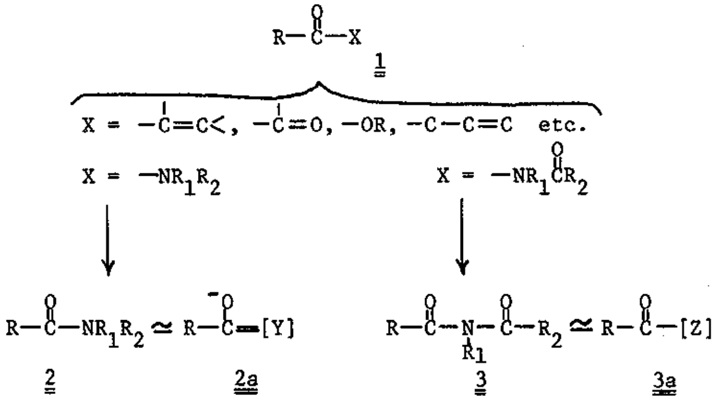
Development and design of novel chromophoric systems and utilization of the special excited-state reactivities lead, by chemical quenching, such as bond formation and fragmentation, to molecular structures which would be not readily accessible by recourse to conventional thermal reactions proceeding through ground-state paths. Although one may have initially viewed photoreactions as nonselective degradations, accumulation of tremendous research effort and development of mechanistic work encouraged synthetic chemists to explore the possible uses of photochemical methods in designing the organic synthesis. Indeed, photoreactions provide avenues for syntheses that are unparalleled by conventional methods.

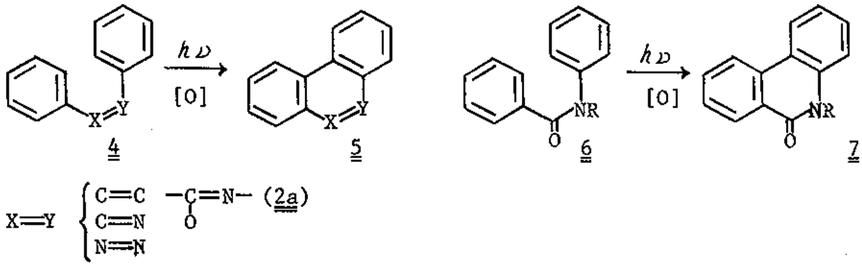
In the literature, a multitude of photoreactions have been extensively documented involving examples of a wide variety of carbonyl derivatives **1**, in which a carbonyl is conjugated with unsaturated or heteroatom systems. In the present paper, an amide group **2** is selected as the first example of the use of such carbonyl derivatives in the synthesis of nitrogen-heterocycles. The second example will be an imide group **3**, whose photochemistry has been originally found and developed in our laboratories.



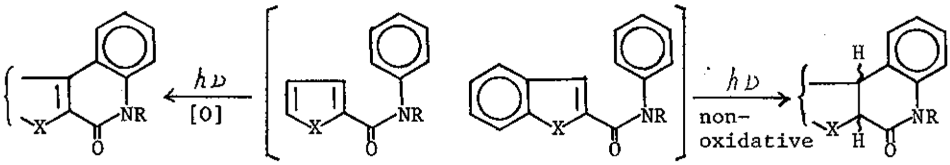
In the amide system **2**, interaction with an amino group decreases the reactivity of the carbonyl and, as a result, amides may behave photochemically like a double bond system **2a**. In the imide system **3**, a cross-conjugated carbonyl system involving a nitrogen, effects of the amino and the second carbonyl groups appear to compensate each other. Therefore, in a rough approximation, excited imides resemble with a simple keto system **3a**.

Such simple models as **2a** and **3a** provide the basis of preliminary synthetic design with these synthon chromophores in this work.

Oxidative photocyclization of stilbenes **4** to phenanthrenes **5** is well known. Replacement of the double bond connecting the two aromatics of stilbenes by an amide group **2a** forms benzanilides **6**. Photochemical transformation of **6** to phenanthridones **7** is in fact known but **7** were reported to be formed only in poor yields. On the basis of improved adaptation of the photocyclization of various anilides, a variety of polyaromatic heterocyclic systems containing quinolones **8** have been synthesized[1].

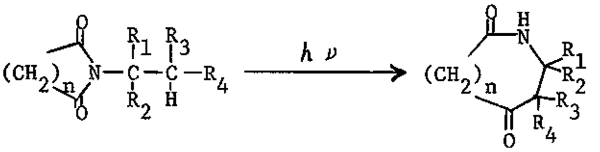


In addition, five-membered heteroaromatic anilides 9, 10 permitted separation of a non-oxidative route from the oxidative one to afford a dihydroquinolone system 11[2]. Based on stereochemical studies of the reaction, a "solvent-mediated" mechanism was proposed as a novel example of participation of the reaction medium in the course of a seemingly concerted reaction.



8 9 10 11

The parallelism of the imide with a simple carbonyl was typically demonstrated by the photochemical behavior of alicylic imides. The principal feature of the Norrish type II processes of the alicyclic imides 12 is that the cyclization is rather dominant leading to ketolactams 13 with ring-enlargement by the two carbon unit derived from the side chain[3].



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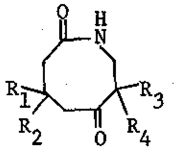
Variation of the N-substituents may lead to a number of new heterocycles. While the ring size of the imides (n) can be increased beyond three, the imide ring may carry substituents including heteroatoms as well as cycloalkanes as desired. In view of their multifunctionality, these photoproducts will be further used as snythetic intermediates. Thus this novel ring expansion has general synthetic potential and will afford an entry to various medium-sized and other heterocyclic systems. Some illustrative examples hitherto synthesized are shown below (14-16).



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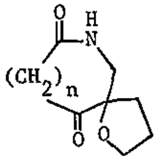

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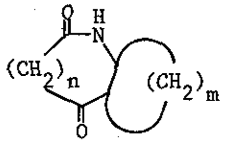

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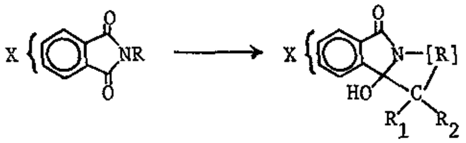
Photoreactions of aromatic cyclic imides, phthalimides 17, are particularly versatile in that extensive type II processes are performed, thus a wide variety of aza-cyclopentanol 18, benzazepinone 19, and other systems are available by the photocyclization of N-substituted phthalimide derivatives via γ- and δ-hydrogen abstraction by the excited imide carbonyl[4].



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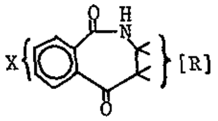

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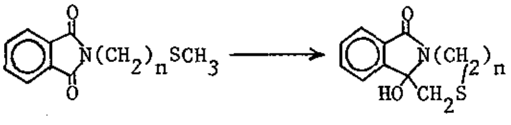
An interesting "synthetic control" has been observed in the behavior of some phthalimides[5]. For example, certain phthalimides 20 possessing a terminal methylthio group undergo a novel regioselective remote photocyclization to give macrocyclic products 21. This technique was applied to synthesis of cyclic peptide models of up to 21-memberd ring. These results strongly encourage the applications of the "photolysis of donor-acceptor pair systems" for general synthetic purposes.



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