

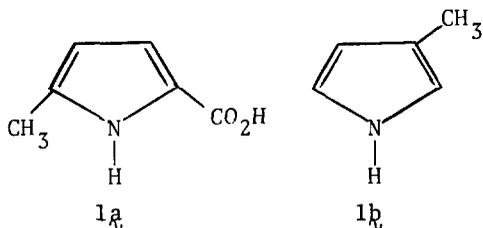
PHOTOCHEMISTRY OF 3,6-DIHYDRO-1,2-OXAZINES  
A VERSATILE ROUTE TO SUBSTITUTED PYRROLES<sup>1</sup>

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**Summary** A high yield pyrrole synthesis which employs a sequence of cycloaddition, photoextrusion of H<sub>2</sub>O and Birch reduction has been developed.

There are few general synthetic routes to substituted pyrroles, especially the 3-substituted derivatives.<sup>2</sup> Most methods provide a specific substitution pattern or yield 2-substituted pyrroles.<sup>2a,b</sup>

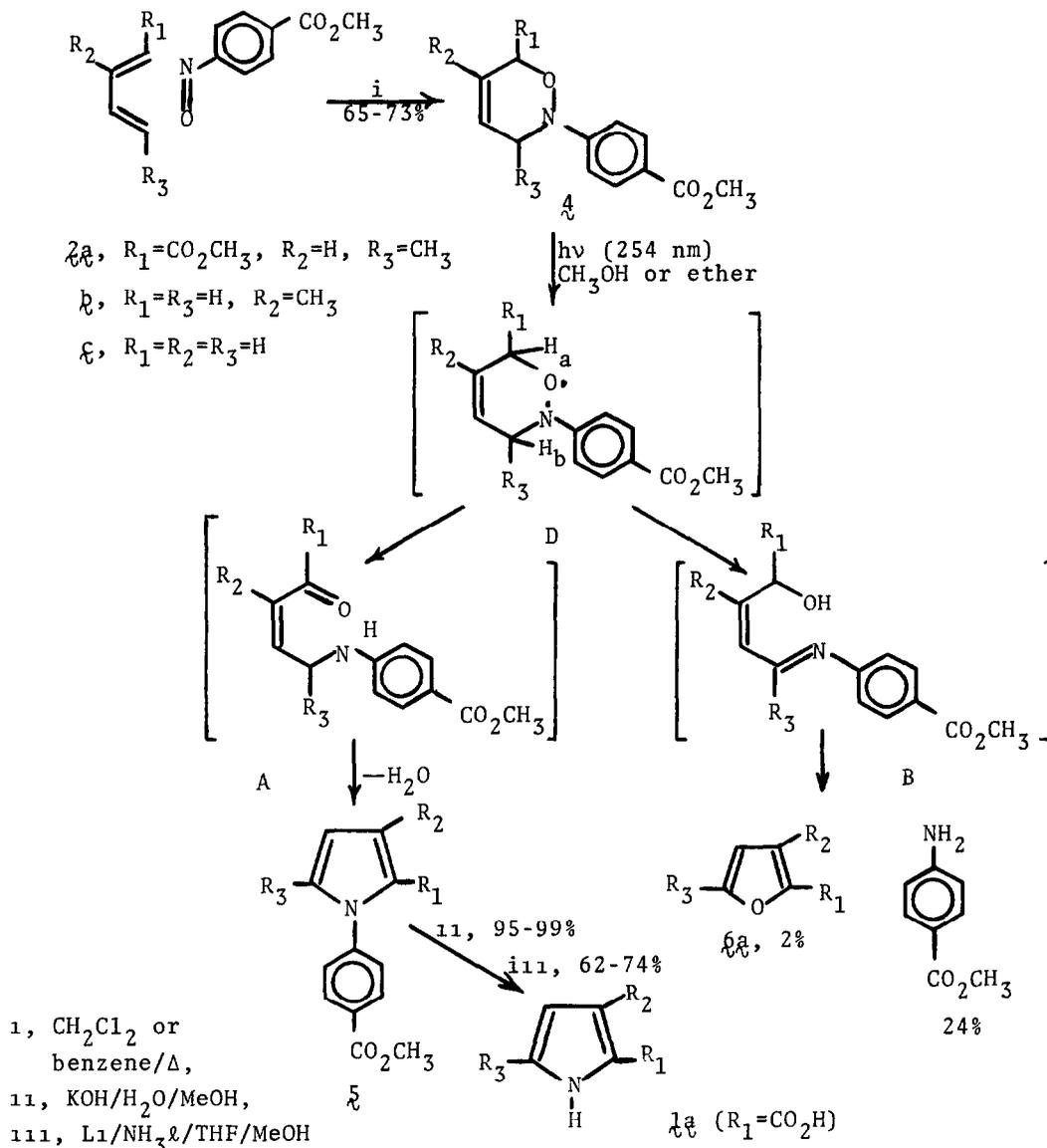
We wish to report a versatile and apparently general photochemical method for synthesizing substituted pyrroles<sup>3</sup> such as those illustrated below. An example of this route is outlined in the four-step sequence shown in the Scheme and has been accomplished in an overall yield of 32% for **1a**. The key



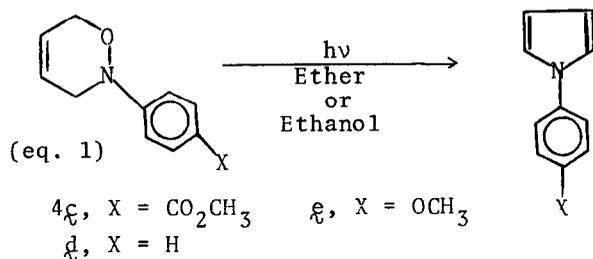
steps are the photoextrusion of H<sub>2</sub>O from the 3,6-dihydro-1,2-oxazine<sup>4</sup> and the removal of the N-aryl group under Birch reduction conditions.<sup>5</sup> Both transformations have been accomplished in good yield.

The choice of methyl *p*-nitrosobenzoate<sup>3</sup> as the source of the pyrrole nitrogen is predicated on three factors: (1) the electronic properties of the dienophile are enhanced by the carbomethoxy group,<sup>6,7</sup> (2) the photochemical extrusion reaction requires a suitable stable chromophore for the absorption and subsequent photochemical homolysis of the N—O bond,<sup>1,4</sup> and (3) the Birch reduction of the aryl group in the hydrolyzed pyrrole acid (**6**) is assured. Furthermore, although two regioisomers of the 1,2-oxazine might be expected from the cycloaddition step,<sup>2a,4,6,7</sup> the subsequent photoextrusion reaction erases this regiochemistry, because the two isomers lead to the same pyrrole.

## Scheme Photochemical Synthesis of Substituted Pyrroles



The mechanism of the photochemical extrusion probably entails homolytic fission of the NO bond to the diradical (D) followed by intramolecular disproportionation to either the unsaturated ketoamine (A) or hydroxy imine (B) as suggested earlier by Scheiner, Chapman, and Lassila.<sup>4</sup> The formation of A is thermodynamically favored by 2 to 6 kcal/mol over B ( $R_1-R_3=H$ ).<sup>8</sup> A small amount of methyl *p*-aminobenzoate and the furan always accompany the pyrrole product indicating the intermediacy of the hydroxy imine B.



A comparison of the effect of aryl substituents on the photochemistry with oxazines  $4c-e$  (eq 1) is shown in Table 1. While the pyrrole appearance efficiencies are relatively constant, the disappearance efficiencies are lower for the substituted oxazines

indicating fewer side reactions. As noted in the Scheme, this photoextrusion step is always accompanied by fragmentation to a substituted aniline (and the corresponding furans).<sup>4</sup>

Table 1. Substituent Effect on the Photoextrusion of H<sub>2</sub>O from N-Aryl-3,6-dihydro-1,2-oxazines ( $4c-e$ ).

Oxazine	Conditions <sup>a</sup>	$\phi_{\text{pyr}}^b$	$\phi_{\text{anil}}^b$	Yield <sup>c</sup>
$4c$	D	0.46	0.28	61%
$4d$	D	0.57	0.30	53%
	S	0.0	0.0	0%
$4e$	D	0.46	0.25	54%

- a) D=Direct irradiation in quartz vessels at 254 nm in ether. Aliquots were taken at 15-min. intervals and analyzed by nmr with an internal standard. S=Sensitized irradiation carried out with acetophenone (0.1M) at 350 nm in benzene-d<sub>6</sub>
- b) Error limits estimated at 10%.
- c) Determined by nmr analysis of the crude reaction mixture. For  $4c$ , yields of isolated pyrrole ranged from 45 to 70% (column chromatography).

In a test of the multiplicity requirements for the extrusion reaction, two of the oxazines were subjected to acetophenone sensitization. For the unsubstituted oxazine  $4d$ , no product and little starting material disappearance was noted. In contrast,  $4a$  was sensitized by acetophenone very efficiently. This observation was in contrast to the observation that both oxazines efficiently quenched acetophenone phosphorescence at room temperature<sup>9</sup> ( $k_{\text{energy transfer}} = 3.5 \pm 1.1 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$  and  $1.4 \pm 0.3 \times 10^9 \text{ M}^{-1}\text{s}^{-1}$  for  $4a$  and  $4d$ , respectively). The lack of reactivity of the unsubstituted oxazine triplet must stem from rapid competing modes of decay.

There are other methods for effecting the extrusion of  $H_2O$  from 1,2-oxazines<sup>7,10</sup> but they lack generality. For example, Kresze has shown that base-catalyzed or alumina-catalyzed dehydration of the p-chloro analog of **4a** gives the corresponding pyrrole in good yield.<sup>2b,7</sup> We have confirmed this for **4a** where treatment with alumina gave **5a** in 84% yield. However, applying this method to **4b** does not yield pyrrole **5b** even at elevated temperatures, an indication that Kresze's method is limited to oxazines with electron withdrawing groups at  $R_1$  also in accord with Sasaki's findings.<sup>6d</sup>

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