

PHOTOARYLATION. I.

PHOTOCHEMICAL SYNTHESIS OF BENZOTHIENO[2,3-c][1,x]DIAZANAPHTHALENE SYSTEMS
BY INTRAMOLECULAR DEHYDROCHLORINATION¹

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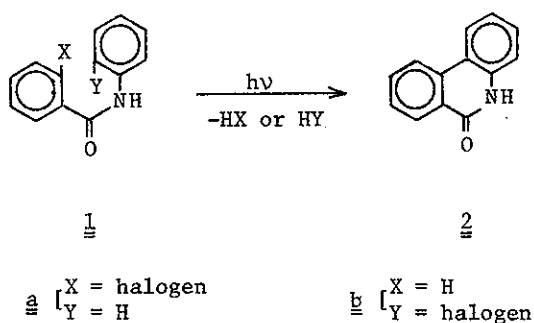
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By intramolecular photoarylation of the amides derived from 3-chlorobenzothiophene-2-carboxylic acid and aminopyridines, novel polycyclic heteroaromatic systems were synthesized. This approach may be employed as a supplemental method for the oxidative photocyclization.

The problem in adapting the photolysis of haloarenes for synthetic purposes has been initially discussed and illustrated by Kharasch *et al.* with iodoaromatics as the typical examples.² Thus the photolysis of iodoaromatic compounds yielded biphenyls, phenanthrenes and other arylated products, and the homolytic nature of the process was established.^{2c} Since then there have been reported many papers in which such photoarylation reactions are employed for syntheses including those of natural products.³

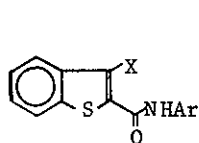
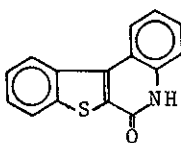
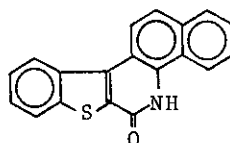
Oxidative photocyclization reactions of anilides have been found earlier again by Kharasch *et al.*,^{2b} studied extensively over the last few years in our

laboratories and have been shown to be potentially valuable in heteroaromatic syntheses.⁴ During the course of our studies it has been revealed that the reaction suffers from serious structure-reactivity dependency. For example, whereas benzoyl derivatives of α - and γ -aminopyridines undergo the cyclization, the β -derivative gave only the photo-Fries products.^{4c} Anilides derived from five-membered heterocyclic carboxylic acids undergo smooth cyclization,^{1a,4a} while those from pyridinecarboxylic acids all resisted the reaction.^{4b} A typical example may be found in the synthetic problems of benzophenanthridine alkaloids, to which much attention has been recently directed with regard to the biological activities manifested by some of the derivatives.⁵ Because the benzoyl derivatives of α -naphthylamine resisted the oxidative photocyclization,^{4b,6} in place of this reaction, intramolecular photoarylation with the bromo derivatives has been successfully employed for the syntheses.^{6,7} In view of such a limitation, we have decided to systematically investigate the photoarylation in an attempt to complement the synthetic scope of the photocyclization.



In connection with the oxidative cyclization, Kharasch *et al.*^{2b} reported photoarylation of simple halo anilides 1 (halogen = iodine). Mondon and Krohn also examined that of the bromo derivatives 1.⁸ Aromatic chloro compounds have been described as photochemically unreactive,^{2c} in contrast to bromo and

iodo compounds, and therefore have attracted less attention. We have started our systematic study with the 3-chloro derivatives of benzothiophene-2-carboxylic acid anilides 3.

345

3a ; Ar = phenyl, X = H
3b ; Ar = α -naphthyl, X = H
3c ; Ar = phenyl, X = Cl
3d ; Ar = α -naphthyl, X = Cl

In preliminary experiments, photoreactions of the anilide 3a and the α -naphthylamide 3b of benzothiophene-2-carboxylic acid were compared with those of the chloro compounds 3c, 3d. While the photolysis of 3a (benzene : ethanol = 10 : 1 ; 2 hr; 100-W high-pressure mercury lamp) gave 4 in 45 % yield,^{4b,9} irradiation of 3c under similar conditions for only 20 min gave 4 in a quantitative yield. Further, the amide 3b gave the pentacyclic compound 5 (mp > 310°) in 30 % yield, upon similar irradiation, whereas the chloro amide 3d readily produced 5 in 74 % yield.

A solution of the chloro amide (6, 9, 12) in ethanol (1 mmol in 500 ml) containing triethylamine (1.1 mmol) was irradiated with a 500-W high-pressure mercury lamp in a Pyrex vessel under an atmosphere of nitrogen for 15-25 min. Products were purified by recrystallization or column chromatography (silica gel), and the results are listed in Table I.¹⁰ Though 6a was stable on standing in ethanol in the dark, on heating at 200° for 4 hr it was converted into 8a (56 %) to establish its structure to be the product of C-N bond for-

mation. The similar thermal reaction of 6b afforded 8b in 77 % yield. Ultraviolet spectral patterns of 7a and 7b, and those of 8a and 8b were nearly superimposable from each other, respectively, in good support of the assigned structures. Photolysis of 9a afforded 10 and 11a, whose structural assignments were mainly based on : (a) NMR ($\text{CF}_3\text{CO}_2\text{D}$) ; δ 8.83 (s, $\text{C}_4\text{-H}$), 8.85 (d, $J=6.5$, $\text{C}_1\text{-H}$) in 10 ; (b) close resemblance of the uv spectrum of 11a to that of 11b, obtained from 9b which has only one site for the cyclization. These results demonstrate that the chloro derivatives of benzothiophene-2-carbox-azanilides (6, 9, 12) undergo smooth photocyclization to afford the corresponding diaz-naphthalene systems. Although it has been known that five-membered hetero-

Table I. Photocyclization Products

| Amide | Time (min) | Products (Yield ^a ; mp ^b) |
|-----------|------------|---|
| <u>6a</u> | 15 | <u>7a</u> (48 %; > 300°, P) <u>8a</u> (15 ; > 300°, E) |
| <u>6b</u> | 15 | <u>7b</u> (50 ; > 300°, P) <u>8b</u> (21 ; 292-3°, E) |
| <u>9a</u> | 25 | <u>10</u> (34 ^c); > 300°, P) <u>11a</u> (48 ^c); > 300°, P) |
| <u>9b</u> | 20 | <u>11b</u> (80 ; > 300°, P) |
| <u>12</u> | 20 | <u>13</u> (91 ; > 300°, P) |

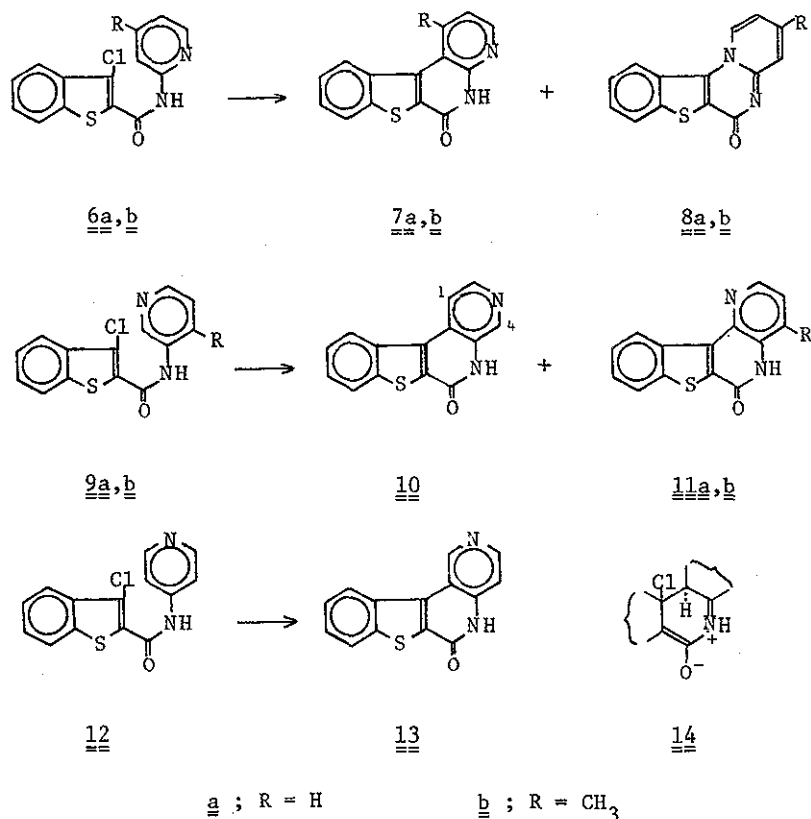
a) yields of purified products unless otherwise stated.

b) recrystallized from pyridine (P) or ethanol (E).

c) yields estimated by NMR.

cyclic carboxanilides such as thiophene-2-, N-methylpyrrole-2- and N-methyl-indole-2-carboxanilides do undergo oxidative photocyclization,^{1a} the photoarylation reaction proceeds more efficiently. For example, the corresponding amide 12 (Cl = H) of γ -aminopyridine gave, on irradiation for 10 hr, 13 only in 6 %

yield.^{4b} Since homolysis of the carbon-chlorine bonds is less likely in view of their bond strength,^{2c,11} a reasonable mechanism may involve, as postulated in the related non-oxidative photocyclizations,^{12,13,14} electrocyclic reaction of the 6 π -arylanilide system to form an intermediate 14, which undergoes irreversible thermal elimination of hydrogen chloride. Further synthetic studies of the photoarylation of the anilides 1 and other systems are under way.



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