

## 2-PYRIDONE RING FORMATION THROUGH THE PHOTOREACTION OF ARENECARBOTHIOAMIDES WITH UNSATURATED CARBOXYLIC ACIDS<sup>1</sup>

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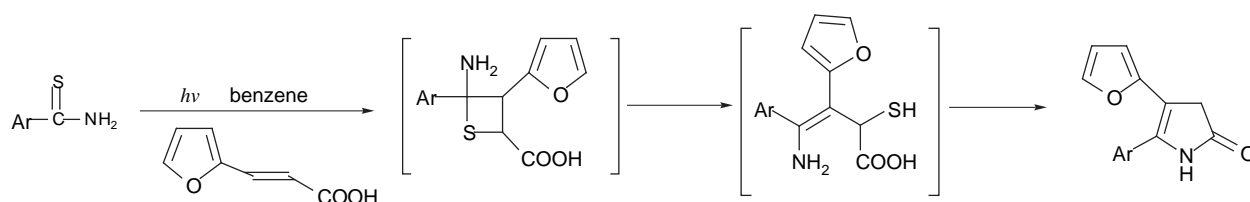
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**Abstract** - Irradiation of arenecarbothioamides with 2,4-hexadienoic acid in benzene gives 2-pyridone derivatives in moderate yields. The corresponding benzo-fused 2-pyridone derivative was also obtained by use of *o*-vinylbenzoic acid as dienic acid equivalent.

2-Pyridones are one of the important classes of heterocyclic compounds that can be found in many biologically active natural products and pharmaceuticals.<sup>2</sup> Therefore, considerable effort has been devoted to the development of synthetic methodology directed at the efficient preparation of 2-pyridone derivatives.<sup>3</sup>

In the course of our systematic study on photochemistry of the arenecarbothioamide-alkene system,<sup>4</sup> we found that photoreaction of arenecarbothioamides with 3-furan-2-ylacrylic acid in benzene proceeds *via* key intermediate 4-amino-3-butenoic acid to give 2,3-diaryl-2-pyrrolin-5-one (scheme 1).<sup>5</sup> From the



Scheme 1

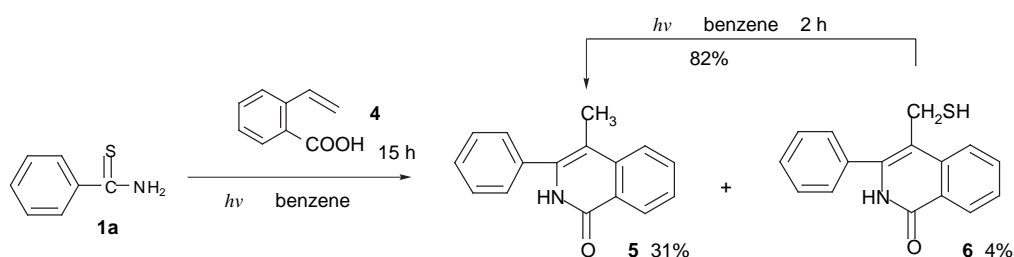
finding of 2-pyrrolin-5-one formation, utilization of a diene-conjugated carboxylic acid as a photochemical substrate for 2-pyridone formation was suggested. In this communication we wish to report a facile synthesis of 6-aryl-2-pyridones and benzo-fused 2-pyridone through the photoreaction of arenecarbothioamides with diene-conjugated carboxylic acids.

Photoreaction of arenecarbothioamides (**1**) with 2,4-hexadienoic acid (**2**) was carried out in benzene using a high-pressure mercury lamp through a Pyrex filter under a nitrogen atmosphere. The results are listed in Table 1. Irradiation of benzenecarbothioamide (**1a**) with 3 eq of **2** for 15 h gave exclusively 6-phenyl-2-pyridone derivative (**3a**: 33%).<sup>6</sup> Further, the photoreactions of a series of heteroaromatic thioamides (**1b-d**) with **2** were performed. As expected, the corresponding 6-aryl-2-pyridones (**3b-d**) were obtained in moderate yields.<sup>7</sup>

Table 1. Photoreaction of **1** with **2**

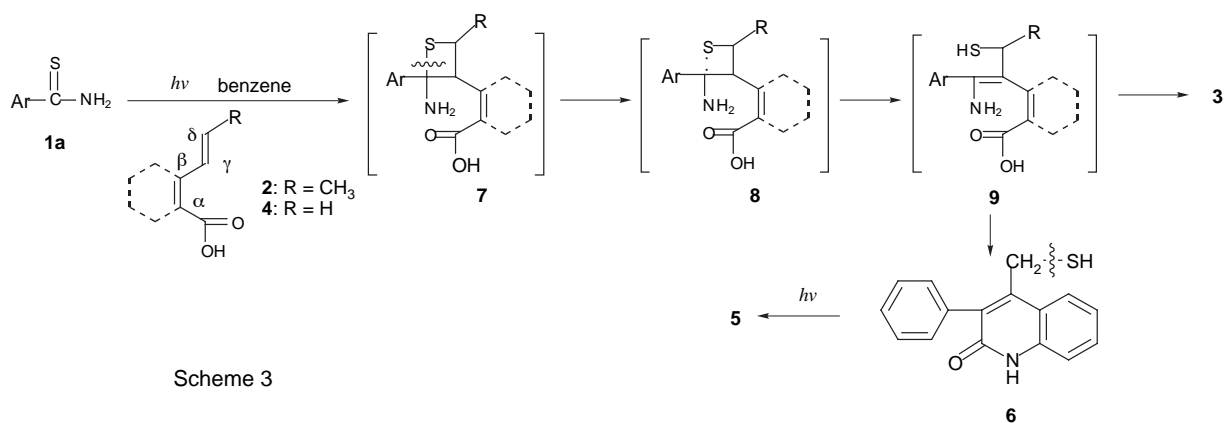
Ar =	1	Irradiation time (h)	3	Yield (%)
		15	<b>3a</b>	33
		20	<b>3b</b>	35
		10	<b>3c</b>	40
		10	<b>3d</b>	37

Next, as an extension of this reaction, *o*-vinylbenzoic acid (**4**) as dienoic acid equivalent was selected. Irradiation of **1a** with **4** for 15 h gave 4-methyl-3-phenyl-2*H*-isoquinolin-1-one (**5**: 31%),<sup>8</sup> accompanied by small amounts of thiol (**6**: 4%).<sup>9</sup> Presumably, the isoquinolinone (**5**) was derived from thiol derivative



Scheme 2

(6). In fact, thiol (6) was easily converted to (5) by further irradiation for 2 h in 82 % yield (Scheme 2). From these experiments, the reaction seems to proceed in several steps involving initial thietane (7) formation between the thiocarbonyl and  $\gamma,\delta$ -alkenyl moiety of 2 or 4, leading to the key  $\omega$ -aminodienoic acid intermediate (9), which subsequently cyclizes to the 2-pyridone derivatives (3) as shown in Scheme 3. However, no evidence is available at this time to suggest if this step (9  $\rightarrow$  3) is thermal or photochemical. Similarly, in the case of *o*-vinylbenzoic acid (4) as dienoic acid analogue, formation of benzo-fused 2-pyridone (5) seems to proceed *via* thiol (6) which arises from the initially formed thietane (7) followed by photochemical fission of the C-S bond of the thietane ring, and then subsequent cyclization.



In summary, the new photochemical formation of 2-pyridones promises to have applications to the synthesis of 6-substituted 2-pyridone and various benzo-fused ones. These results also demonstrate that certain dienoic acid and its analogues are a potentially useful building block in photosynthesis of nitrogen-containing heterocycles. We are currently investigating on further synthetic application and reaction pathway of this reaction.

## ACKNOWLEDGEMENTS

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- 6-Phenyl-4-sulfanylethyl-1*H*-pyridin-2-one (**3a**): colorless oil; IR (Nujol) 3380, 1660  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  1.49 (d, 3H,  $J=7.0$  Hz), 1.87 (d, 1H,  $J=4.0$  Hz), 4.13 (m, 1H), 6.52 (d, 1H,  $J=9.6$  Hz), 7.4-7.5 (m, 5H), 7.68 (d, 1H,  $J=9.6$  Hz), 11.33 (br s, 1H);  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  25.8 (q), 33.1 (d), 120.3 (d), 120.9 (s), 128.7 (dx2), 128.9 (dx2), 129.9 (d), 132.9 (s), 140.4 (d), 142.8 (s), 163.5 (s); MS  $m/z$  231 ( $\text{M}^+$ ); HRMS Calcd for  $\text{C}_{13}\text{H}_{13}\text{NOS}$ : 231.0718. Found: 231.0711.
- The progress of photolysis was monitored by thin layer chromatography (TLC) until the arenecarbothioamide (**1**) was disappeared. Their photoproducts (**3**) were obtained as sole product accompanied by inseparable polymer at the bottom of reaction vessel.
- 4-Methyl-3-phenyl-2*H*-isoquinolin-1-one (**5**): mp 209-211 $^\circ\text{C}$ ; IR (Nujol) 3160, 1650  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  2.27 (s, 3H), 7.4-7.6 (m, 6H), 7.75 (m, 2H), 8.45 (d, 1H,  $J=8.1$  Hz), 9.02 (br s, 1H);  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  13.9 (q), 109.2 (s), 123.7 (d), 125.4 (s), 126.4 (d), 127.8 (d), 128.8 (dx2), 129.1 (d), 129.2 (dx2), 132.8 (d), 135.4 (s), 136.6 (s), 138.8 (s), 162.5 (s); MS  $m/z$  235 ( $\text{M}^+$ ); HRMS Calcd for  $\text{C}_{16}\text{H}_{13}\text{NO}$ : 235.0997. Found: 235.1004.
- 3-Phenyl-4-sulfanylmethyl-2*H*-isoquinolin-1-one (**6**): colorless oil; IR (Nujol) 3380, 1660  $\text{cm}^{-1}$ ;  $^1\text{H}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  1.71 (t, 1H,  $J=7.3$  Hz), 3.69 (d, 2H,  $J=7.3$  Hz), 7.4-7.6 (m, 6H), 7.7 (m, 2H), (m, 1H), 9.11 (br s, 1H);  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ )  $\delta$  24.2 (t), 109.9 (s), 124.4 (d), 125.7 (s), 127.9 (d), 128.1 (d), 128.8 (dx2), 129.6 (d), 130.5 (dx2), 132.8 (d), 136.2 (s), 137.0 (s), 138.4 (s), 162.5 (s); MS  $m/z$  267 ( $\text{M}^+$ ); HRMS Calcd for  $\text{C}_{16}\text{H}_{13}\text{NOS}$ : 267.0718. Found: 267.0711.