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Pyridine ring formation through the photoreaction of arenecarbothioamides with diene-conjugated carbonyl compounds†

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Irradiation of arenecarbothioamides with hexa-2,4-dienal in benzene solution gives 2-arylpyridines in moderate yields.

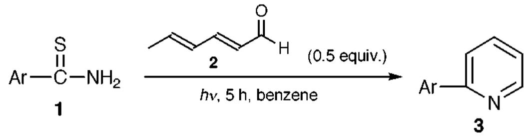
Of all the naturally occurring heterocycles, the pyridine ring is one of the most well-known simple structures. Pyridine and fused-pyridine moieties are present in numerous natural products, such as the quinoline and isoquinoline alkaloids,[2] and have a vast range of potential biological activities. Therefore, many methods for pyridine ring formation have been reported.[3] In addition, in fields other than the biological one, synthetic methods for pyridine derivatives were also required and developed. Since di- and tri-heteroaromatic compounds[4] containing pyridine have received significant attention in the fields of electrical materials,[5] biologically active molecules,[6] chelating agents and metal–ligand chemistry,[7] the synthesis of arylpyridine derivatives has become increasingly important.

In the course of our systematic study of the photochemistry of the arenecarbothioamide–alkene system,[8] we found that photoreaction of arenecarbothioamides with 2-furylacrylaldehyde in benzene proceeds *via* key intermediate 4-aminobut-3-enal to give 2,3-diarylpyrrole derivatives.[9] From this pyrrole formation, utilization of a diene-conjugated carbonyl as a photochemical substrate for pyridine formation was suggested. Here we report a facile synthesis of 2-arylpyridines, 2,6-diarylpyridines and benzo-fused pyridines through the photoreaction of arenecarbothioamides with diene-conjugated carbonyl compounds.

Photoreaction of arenecarbothioamide **1** with hexa-2,4-dienal **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 0.5 equiv.[10] of **2** for 5 h exclusively gave 2-phenylpyridine **3a** (32%). Further, the photoreactions of a series of heteroaromatic thioamides **1b**–**f** with **2** were performed. As expected, the corresponding 2-arylpyridines **3b**–**f** were obtained in moderate yields.

In addition, preparation of 2,6-diarylpyridines was also examined. The photolysis of arenecarbothioamide **1** with 1-arylhexa-2,4-dien-1-one **4** was carried out under similar conditions to those described above. Similarly, the expected 2,6-diarylpyridines **5** were obtained in moderate yields (Table 2).

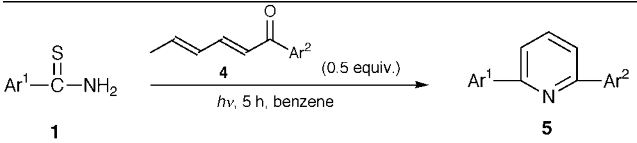
Table 1 Photoreaction of arenecarbothioamides **1** with hexa-2,4-dienal **2**



1	Ar		Yield (%)
1a	Ph	**3a**[a]	32
1b	3-pyridyl	**3b**[a]	34
1c	4-pyridyl	**3c**[a]	28
1d	2-furyl	**3d**[b]	35
1e	3-furyl	**3e**[b]	30
1f	2-thienyl	**3f**[c]	37

[a] See ref. 11. [b] See ref. 4. [c] See ref. 12.

Table 2 Photoreaction of arenecarbothioamides **1** with 1-arylhexa-2,4-dien-1-one **7**

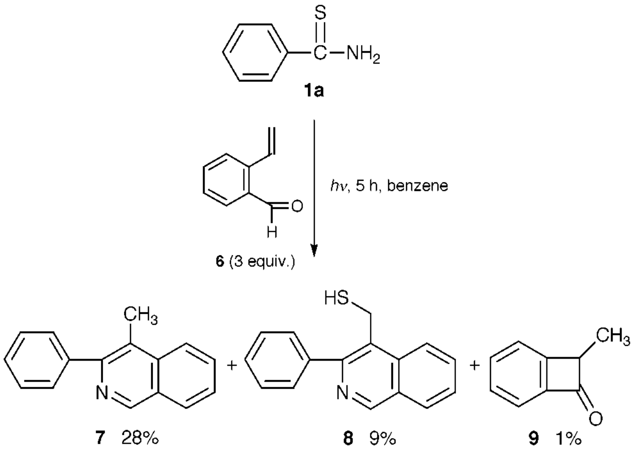


1	Ar^1	4	Ar^2		Yield (%)
1a	Ph	**4a**	Ph	**5a**[a]	32
1a	Ph	**4b**	3-pyridyl	**5b**	34
1a	Ph	**4c**	2-furyl	**5c**	28
1a	Ph	**4d**	2-thienyl	**5d**[b]	35
1d	2-furyl	**4c**	2-furyl	**5e**	30
1f	2-thienyl	**4d**	2-thienyl	**5f**[b]	37

[a] See ref. 13. [b] See ref. 14.

Next, as an extension of this reaction, photoreaction of **1a** with *o*-vinylbenzaldehyde **6** as the dienal equivalent was performed under similar conditions. Irradiation of **1a** with **6** for 5 h gave 4-methyl-3-phenylisoquinoline[15] **7** (28%) and (3-phenyl-4-isoquinolyl)methanethiol **8** (9%), accompanied by small amounts of **9** (Scheme 1).[16] Presumably, the isoquinoline **7** was derived from thiol derivative **8**. In fact, thiol **8** was easily converted to **7** by further irradiation.

From these experiments, the reaction seems to proceed in several steps involving initial thietane **10** formation between the thiocarbonyl and γ,δ-alkenyl moiety of **2**, leading to the key ω-aminodienal intermediate **12**,[17] which subsequently cyclizes to the pyridine derivatives **3** as shown in Scheme 2 (pathway A). However, no evidence is available at this time to suggest if this step is thermal or photochemical. In the case of *o*-vinylbenzaldehyde **6** as dienal analogue, formation of isoquinoline **7**



Scheme 1

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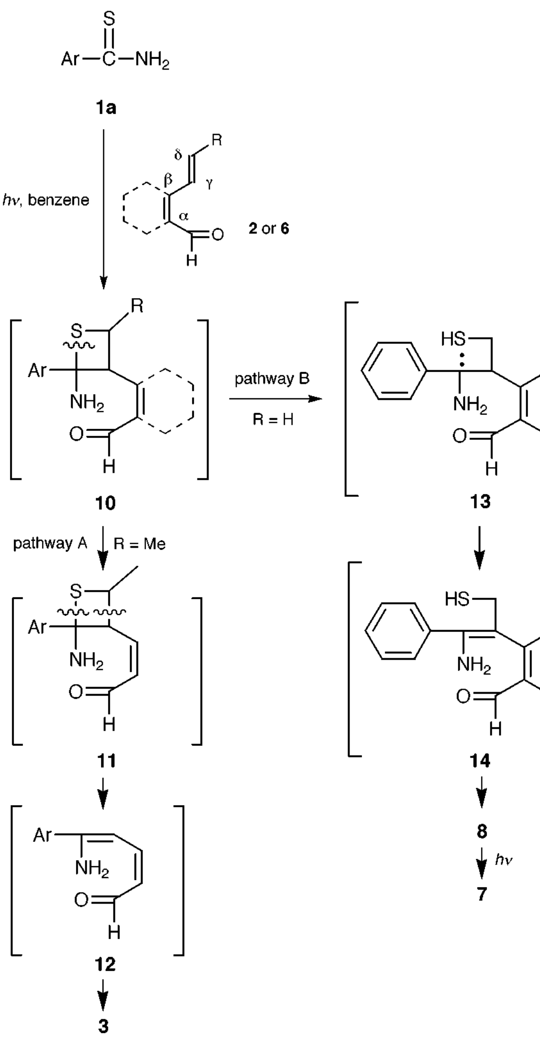
† Photochemistry of the Nitrogen–Thiocarbonyl Systems. Part 34. For Part 33, see ref. 1.



Scheme 2

seems to proceed *via* thiol **8** which arises from the initially formed thietane **10** followed by photochemical fission of the C–S bond of the thietane ring, and then subsequent cyclization (pathway B).

In this study, the new photochemical formation of pyridine promises to have broad applications for the synthesis of aryl- and heteroaryl-pyridines. In addition, it was shown that certain dienal species and their analogues are potentially useful building blocks in photosynthesis of nitrogen-containing heterocycles. A detailed study on further synthetic application and the reaction pathway of this reaction is in progress.

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10 To avoid formation of the photodimer of **2**, the molar ratio of **1a** and **2** was varied. As a result, the yield of **3a** increased to 32% using a ratio of 2:1.

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