HETEROCYCLES, Vol. 56, 2002, pp. 69-72, Received, 24th May, 2001

2-PYRIDONE RING FORMATION THROUGH THE PHOTOREACTION OF ARENECARBOTHIOAMIDES WITH UNSATURATED CARBOXYLIC ACIDS[1]

Kazuaki Oda,* Rikiji Nakagami, Naozumi Nishizono, and Minoru Machida

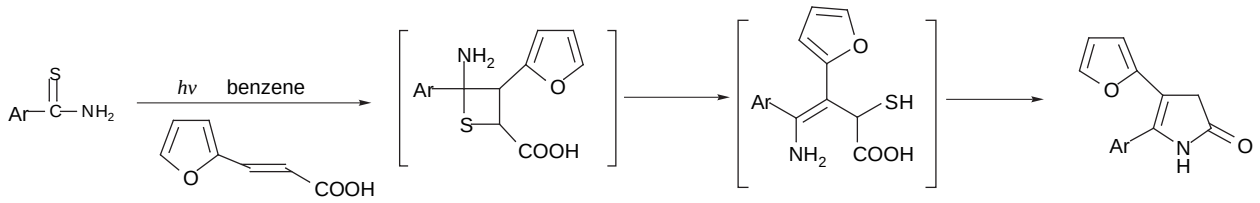
Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido 061-0293, Japan

e-mail: k-oda@hoku-iryo-u.ac.jp

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 dienoic 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.[2] Therefore, considerable effort has been devoted to the development of synthetic methodology directed at the efficient preparation of 2-pyridone derivatives.[3]

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

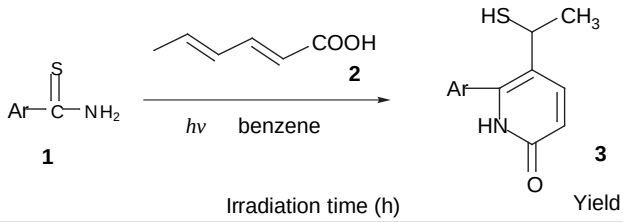


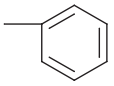
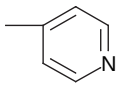
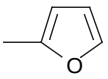
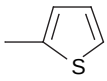
Scheme 1

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.

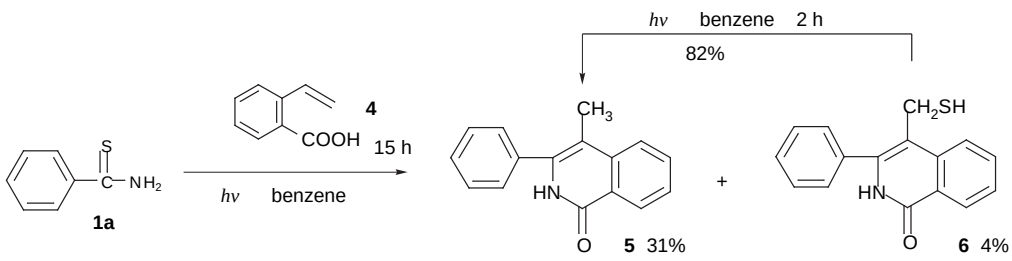
Photoreaction of arenecarbothioamides (**1**) with 2,4-hexadienoic acid (**2**) was carried out in benzene using a high-pressure mercury lamp through a Pyrex filter under a nitrogen atmosphere. The results are listed in Table 1. Irradiation of benzenecarbothioamide (**1a**) with 3 eq of **2** for 15 h gave exclusively 6-phenyl-2-pyridone derivative (**3a**: 33%).[6] 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.[7]

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



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

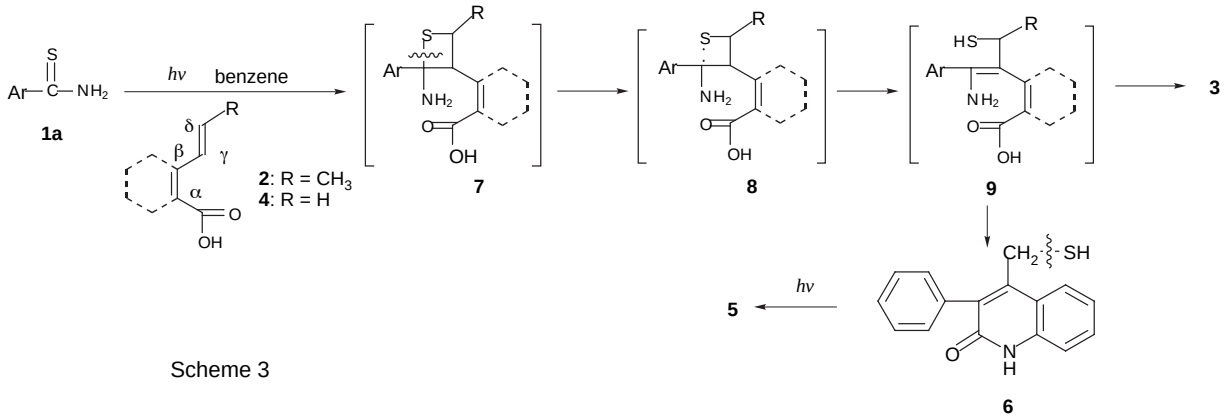
Next, as an extension of this reaction, *o*-vinylbenzoic acid (**4**) as dienoic acid equivalent was selected. Irradiation of **1a** with **4** for 15 h gave 4-methyl-3-phenyl-2*H*-isoquinolin-1-one (**5:** 31%),[8] accompanied by small amounts of thiol (**6:** 4%).[9] Presumably, the isoqunolinone (**5**) 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 γ,δ-alkenyl moiety of **2** or **4**, leading to the key ω-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** **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.



Scheme 3

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

This work was supported in part by Grant-in-Aid for High Technology Research Programs from the Ministry of Education, Culture, Sports, Science and Technology in Japan. We are grateful to Center for Instrumental Analysis, Hokkaido University for measurement of HRMS spectra.

REFERENCES AND NOTES

1. Photochemistry of the Nitrogen-Thiocarbonyl Systems. Part 36. Part 35: K. Oda, T. Ishioka, Y. Fukuzawa, N. Nishizono, and M. Machida, *Heterocycles*, 2000, **53**, 2781.

2. J. M. Mellor, 'Rodd's Chemistry of Carbon Compounds,' Second supplements to 2nd edition of Vol. IV, ed. by M. Sainsbury, Elsevier, Amsterdam, 1998, pp. 416-421.
3. O. Meth-Cohn and K. T. Westwood, *J. Chem. Soc., Perkin Trans. 1*, 1984, 1173; J. Buck, J. P. Madeley, and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1992, 67; S. Mabic and N. Castagnoli, Jr., *J. Org. Chem.*, 1996, **61**, 309.
4. K. Oda and M. Machida, *J. Chem. Soc., Chem. Commun.*, 1994, 1477; K. Oda, H. Tsujita, K. Ohno, and M. Machida, *J. Chem. Soc., Perkin Trans. 1*, 1995, 2931; K. Oda, R. Hiratsuka, and M. Machida, *Heterocycles*, 1996, **43**, 463; K. Oda, M. Sakai, and M. Machida, *Chem. Pharm. Bull.*, 1997, **45**, 584; K. Oda, M. Sakai, H. Tsujita, and M. Machida, *Synth. Commun.*, 1997, **27**, 1183; K. Oda, R. Nakagami, N. Nishizono, and M. Machida, *Chem. Commun.*, 1999, 2371.
5. K. Oda, H. Tsujita, M. Sakai, and M. Machida, *Chem. Pharm. Bull.*, 1998, **46**, 1522.
6. 6-Phenyl-4-sulfanylethyl-1*H*-pyridin-2-one (**3a**): colorless oil; IR (Nujol) 3380, 1660 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 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}C-NMR ($CDCl_3$) δ 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 (M^+); HRMS Calcd for $C_{13}H_{13}NOS$: 231.0718. Found: 231.0711.
7. 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.
8. 4-Methyl-3-phenyl-2*H*-isoquinolin-1-one (**5**): mp 209-211°C; IR (Nujol) 3160, 1650 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 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}C-NMR ($CDCl_3$) δ 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 (M^+); HRMS Calcd for $C_{16}H_{13}NO$: 235.0997. Found: 235.1004.
9. 3-Phenyl-4-sulfanylmethyl-2*H*-isoquinolin-1-one (**6**): colorless oil; IR (Nujol) 3380, 1660 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 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}C-NMR ($CDCl_3$) δ 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 (M^+); HRMS Calcd for $C_{16}H_{13}NOS$: 267.0718. Found: 267.0711.