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Photoreaction of Arenecarbothioamides with 5-Membered Heteroaromatics.[1] The Regioselective Photoinduced Aroylation at the 3-Position of 5-Membered Heteroaromatics

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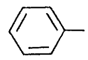
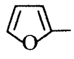
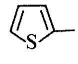
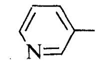
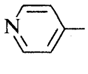
Irradiation of arenecarbothioamide with 5-membered heteroaromatics, including benzo-fused 5-membered ones, gave regioselectively the corresponding 3-aroyl derivatives.

Keywords photoacylation; Paterno–Büchi reaction; thietane; arenecarbothioamide; furan derivative

An effective means of introducing an acyl group into an aromatic ring is the Friedel–Crafts acylation, which is the most general and useful method for the preparation of arylketones. For example, in a preparation of aroylfurans,[2] an acyl group is introduced regioselectively at the 2-position of an unsubstituted furan, but not at the 3-position. During the course of our systematic studies on the photochemistry of thioamide[3] and thioimide[4] systems, we have found that arenecarbothioamides undergo the Paterno–Büchi type reaction with various olefins, such as nonconjugated olefins,[3a,c] styrene derivatives,[3d] and furans,[3b] to give a variety of arylketones. In particular, photoreaction of arenecarbothioamide with furans efficiently and regioselectively gave 3-aroylfurans. Very recently, an efficient acylation at the 3-position of furan *via* tributyl (3-furyl) stannane was reported by Bailey.[5] That has prompted us to report some further results on the generality of the photoinduced aroylation of arenecarbothioamide with 5-membered heterocycles. The present report is a full account of our work on the photoinduced aroylation to 5-membered heteroaromatics, including benzo-fused 5-membered ones.

Photoreactions of arenecarbothioamides (**1**, **2**) with 5-membered heteroaromatics were carried out in benzene using a high pressure mercury lamp through a Pyrex filter under a nitrogen atmosphere. The results are listed in Table I. Irradiation of **1** with 20 eq of furan (**3a**) for 2 h gave exclusively 3-benzoylfuran (**5a**) in 72% yield. Upon irradiation for 5 h, the yield increased slightly to 78%, but more prolonged irradiation caused decomposition of the photoproduct. In the cases of substituted furans such as 2-methylfuran (**3b**) and 2,5-dimethylfuran (**3c**), irradiation for 20 h was required, providing 4-benzoyl-2-methylfuran (**5b**) and 3-benzoyl-2,5-dimethylfuran (**5c**) in 71% and 64% yields, respectively. In the case of thiophene (**3d**) as an olefin analogue (Paterno–Büchi acceptor), the expected 3-benzoylthiophene was obtained in 59% yield, while with pyrrole (**3e**), 3-benzoylpyrrole was not isolated even after irradiation for 20 h and unchanged **1** was recovered. This lack of

TABLE I. Photoreactions of Arenecarbothioamide with 5-Membered Heteroaromatics

Thioamide	Ar=	Heteroaromatic			3	Mole ratio (3 or 4/1 or 2)	Irra. time (h)	Product	Yield (%)
		X	R^1	R^2					
1		O	H	H	(3a)	20	2	**5a**	72
							5		78
		O	H	CH_3	(3b)	20	10	**5b**	45
							20		71
		O	CH_3	CH_3	(3c)	20	10	**5c**	48
							20		64
		S	H	H	(3d)	20	10	**5d**	47
							20		59
		NH	H	H	(3e)	20	20	None	
		$NCOCH_3$	H	H	(3f)	2	20	**5f**	76
2a		O	H	H	(3a)	20	10	**6a**	39
							20		70
2b		O	H	H	(3a)	20	10	**6b**	44
							20		58
2c		O	H	H	(3a)	20	10	**6c**	38
							20		69
2d		O	H	H	(3a)	20	10	**6d**	31
							20		66
1		Benzofuran (**4a**: X=O)				5	20	**7a**	74
1		Benzothiophene (**4b**: X=S)				5	20	**7b**	55

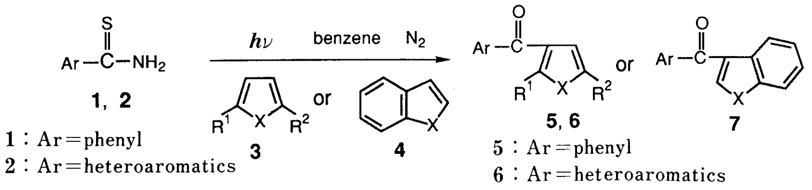


Chart 1

Table II. Physical Data for Photoproducts (**5**, **6** and **7**)

Product	Appearance	mp (°C)	Formula	Analysis (%) Calcd C	H	N	Found C	H	N
5a	Colorless plates	37—38 (lit.[5], 38—39)							
5b	Yellow oil		$C_{12}H_{10}O_2$	77.40	5.41		77.19	5.54	
5c	Yellow oil[6]								
5d	Colorless prisms	64—65 (lit.[8], 64.5)							
5f	Colorless needles	95—96	$C_{13}H_{11}NO_2$	73.22	5.20	6.57	73.51	5.23	6.79
6a	Colorless prisms	58—59 (lit.[5], 57—59)							
6b	Colorless prisms	46—47 (lit.[5], 46—48)							
6c	Colorless prisms	110—111	$C_{10}H_7NO_2$	69.36	4.07	8.09	69.41	4.00	8.02
6d	Colorless prisms	79.5—80	$C_{10}H_7NO_2$	69.36	4.07	8.09	69.58	4.25	8.11
7a	Colorless prisms	64—65 (lit.[9], 63)							
7b	Yellow oil[10]								

Table III. Spectral Data for Photoproducts (**5** and **6**)

Compd.	IR (cm^{-1})	MS (*m/z*)	^{1}H-NMR ($CDCl_3$) δ	^{13}C-NMR ($CDCl_3$) δ
5b	1650	186 (M^+)	2.33 (3H, s), 6.47 (1H, s), 7.4—7.6 (3H, m), 7.75 (1H, s), 7.8—7.9 (2H, m)	13.3 (q), 105.9 (d), 128.5 (d × 2), 128.7 (d × 2), 132.2 (d), 139.0 (s), 147.3 (d), 154.0 (s), 189.5 (s)
5f	1700; 1650	213 (M^+)	2.57 (3H, s), 6.87 (1H, m), 7.33 (1H, m), 7.44—7.48 (3H, m), 7.77 (1H, s), 7.82 (2H, d, J=8.3 Hz)	22.1 (q), 113.4 (d), 120.2 (d), 124.8 (d), 127.4 (s), 128.3 (d × 2), 128.7 (d × 2), 132.0 (s), 138.5 (s), 167.7 (s), 190.3 (s)
6c	1650	173 (M^+)	6.9—7.0 (1H, m), 7.4—7.6 (2H, m), 7.9—8.2 (1H, m), 8.7—8.9 (1H, m), 9.0—9.1 (1H, m)	109.9 (d), 123.6 (d), 126.3 (s), 134.3 (s), 136.1 (d), 144.4 (d), 148.8 (d), 149.6 (d), 152.9 (d), 187.3 (s)
6d	1650	173 (M^+)	6.9—7.0 (1H, m), 7.5—7.7 (3H, m), 7.9—8.0 (1H, m), 8.7—8.9 (2H, m)	109.6 (d), 121.8 (d × 2), 125.9 (s), 144.5 (d), 145.1 (s), 149.2 (d), 150.5 (d × 2), 187.7 (s)

photoreactivity of pyrrole toward thiocarbonyl may be caused by a quenching effect on the excited thioamide by the non-bonding electrons on the heteroatom in pyrrole.[6] But the photoreactivity was restored by 1-acetylation of pyrrole. Irradiation of **1** and 2 eq of 1-acetylpyrrole (**3f**) for 20 h gave exclusively 1-acetyl-3-benzoylpyrrole (**5f**) in 76% yield. With a series of heteroaromatic thioamides (**2a**—**d**), the corresponding 3-aroylfurans (**6a**—**d**) were obtained. In order to examine the generality of this reaction, photoreaction of **1** with benzo-fused 5-membered compounds (**4a**, **b**) as olefin analogues was performed under similar conditions. As expected, 3-benzoyl derivatives (**7a**, **b**) were obtained in moderate yields.

The structures of the products **5a**,[5] **5c**,[7] **5d**,[8] **6a**,[5] **6b**,[5] **7a**,[9] and **7b**[10] were confirmed by comparison of spectral and physical data with reported values. The structures of **5b**, **5f**, **6c**, and **6d** were determined on the basis of the spectral data. For example, in the IR spectrum of **6c**, the absorption band due to a carbonyl group appeared at 1650 cm^{-1}. The ^{13}C-NMR spectrum of **6c** also supported the presence of a carbonyl group [187.3 ppm (s)] and pyridine and phenyl rings.

The formation of **5**, **6**, and **7** may be explained as illustrated in Chart 2. Arylketones (**5**) arise from the initially formed thietanes (**9**) followed by photochemical fission of the C–S bond of the thietane ring, and then by hydrolysis of the generated imines (**10**) during its work-up, such as chromatography. The thietane formation may be explained in terms of the intermediary biradical (**8a**) by analogy with the photoreactions of thioimide systems.[4] The regioselective formation of **5** (3-benzoyl derivatives, not 2-benzoyl derivatives) seems to reflect the stability of the generated biradical (**8a**), which should be more stable than **8b**.

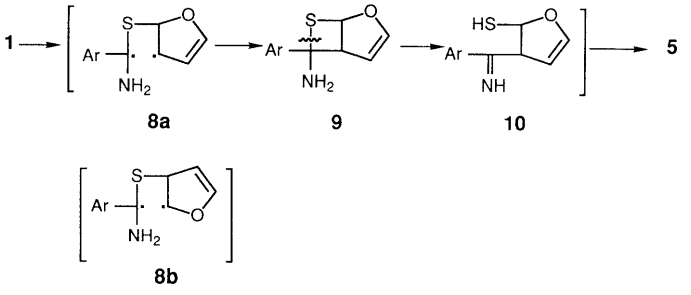


Chart 2

Since furans generally undergo electrophilic substitution, with exceptional ease at the 2-position, direct 3-acylation has heretofore been restricted to a few examples.[5,8]

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3-acylfurans[11] have been reported, few have broad synthetic utility. The methodology described here offers a mild and regioselective means to introduce an aroyl group at the 3-position on five-membered heteroaromatics, and has proven to be of considerable synthetic utility for preparation of naturally occurring 3-substituted furans.[12]

Experimental

All melting points were determined on a Yamato melting point apparatus (model MP-21) and are uncorrected. IR spectra were recorded on JASCO A-102 spectrometer. NMR spectra were taken on JEOL JNM FX-90Q and JEOL JNM EX-400 spectrometers. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane (TMS) (0.0 ppm) as an internal standard. The abbreviations used are as follows: s, singlet; d, doublet; q, quartet; m, multiplet. Mass spectra (MS) were obtained on a JEOL JMS-QH-100 gas chromatograph-mass spectrometer. Preparative irradiations were conducted by using a 1 kW high-pressure mercury lamp (Eikosha EHB-W-1000) through a Pyrex filter at room temperature. Stirring of the reaction mixture was effected by the introduction of a stream of nitrogen at the bottom of the outer jacket. Column chromatography was conducted using silica gel (Merck, Kieselgel 60, 70—230 mesh).

Preparation of Thioamide Derivatives (1, 2) Thioamide derivatives (**1**, **2c**, and **2d**) were commercial products, and other thioamides were prepared by the reported procedure.[3c]

Irradiation of Thioamides (1, 2); General Procedure A solution of **1** (5 mmol) and **2a** (0.1 mol) in benzene (500 ml) was irradiated for 2 h with a 1 kW high-pressure mercury lamp through a Pyrex filter under N_2 at room temperature. After removal of the solvent *in vacuo*, the residue was chromatographed over silica gel. The results are listed in Tables I, II, and III.

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