PHOTOREACTION OF ARENECARBOTHIOAMIDES WITH FURAN. FACILE SYNTHESIS OF PENTAGONAL DI- AND TRI-HETEROCYCLIC COMPOUNDS[1]

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Abstract --- Irradiation of arenecarbothioamides with furan in methanol gave 2-arylpyrrole derivatives in moderate yields. This reaction was applied to the synthesis of pentagonal di- and tri-heterocyclic compounds.

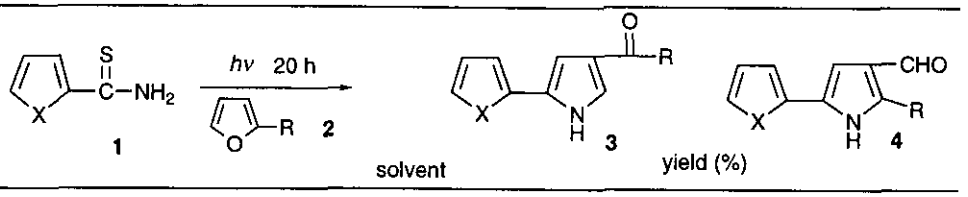
Porphyrin analogs, abiological porphyrin-like systems whose frameworks are expanded, fused, or heteroatom substituted, play important roles in fields not only of electronic materials which have electrical and optical properties,[2] but also of biochemistry and a variety of biomedical applications to anion chelation and drug delivery.[3] Although a great deal of effort in recent years has been devoted toward the syntheses of porphyrin analogs,[4] syntheses of porphyrin-like systems containing heterocyclic units in the place of pyrroles[2,5] also remains of interest. Therefore, for a general and facile synthesis of porphyrin analogs, some of di- and tri-heterocyclic compounds have been required as useful units (precursors).

In the course of our systematic study on the photochemistry of the arenecarbothioamide-furan systems,[6] we have reported a new type of pyrrole-construction reaction.[7] In this paper we wish to report a facile synthesis of pentagonal di- and tri-heterocyclic compounds containing pyrrole ring through photoreaction of arenecarbothioamides with furan.

As has already been reported, photoreaction of arenecarbothioamide with furan in benzene resulted in the formation of 3-aroylfuran.[8] In the case of the same substrates in methanol, irradiation afforded an alternate photoproduct, 5-(2-furyl)pyrrole (**3a**) or 5-(2-thienyl)pyrrole (**3b**) derivative in 68 % or 65 % yield, respectively. Surprisingly, in the photoreaction of 2-pyrrolecarbothioamide (**1c**) with furan, pyrrole-construction reaction occurred even in a benzene solution in the place of a methanol solution, and 5-pyrrol-2-ylpyrrole-3-carbaldehyde (**3c**) was obtained in 48 % yield. Similarly, in photoreaction of **1c** with a series of furan derivatives in benzene, the corresponding 5-(pyrrol-2-yl)pyrrole derivatives (**3**, **4**) were also obtained in moderate yields (Table 1).

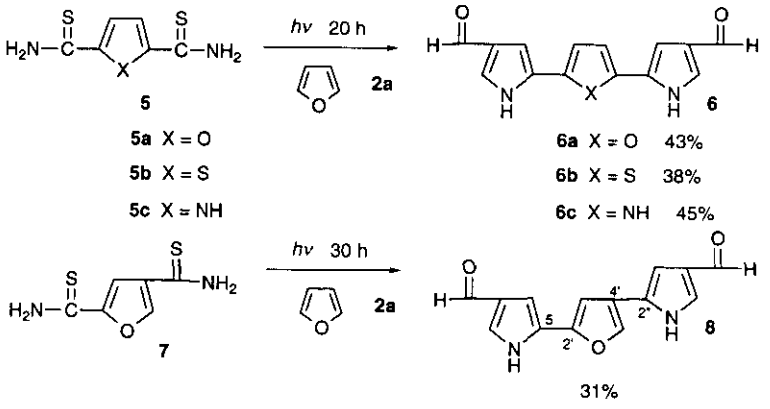
Next, construction of pentagonal triheterocyclic compounds was examined. The photolysis of 2,5-furandicarbothioamide (**5a**) with furan (**2a**) (20 eq.) was carried out in a methanol solution under similar

Table 1. Photoreaction of 1 with 2.



1a	X = O	**2a** R = H	methanol	**3a** 68	—
1b	X = S	**2a** R = H	methanol	**3b** 65	—
1c	X = NH	**2a** R = H	benzene	**3c** 48	—
1c	X = NH	**2b** R = Ph	benzene	**3d** 44	—
1c	X = NH	**2c** R = OCH_3	benzene	**3e** 39	**4e** 12
1c	X = NH	**2d** R = OPh	benzene	**3f** 44	**4f** 9

conditions described above. As expected, 5-[5-(4-formylpyrrol-2-yl)-2-furyl]pyrrole-3-carbaldehyde (**6a**) was obtained in 43% yield. Similarly, with 2,5-thiophenedicarbothioamide (**5b**) (or 2,5-pyrroledicarbothioamide (**5c**)), the corresponding extended triheterocyclic compound was obtained in 38% (or 45%). Using 5-membered 2,4-dicarbothioamide (**7**) as photochemical substrates, a 5,2',4',2''-system[9]

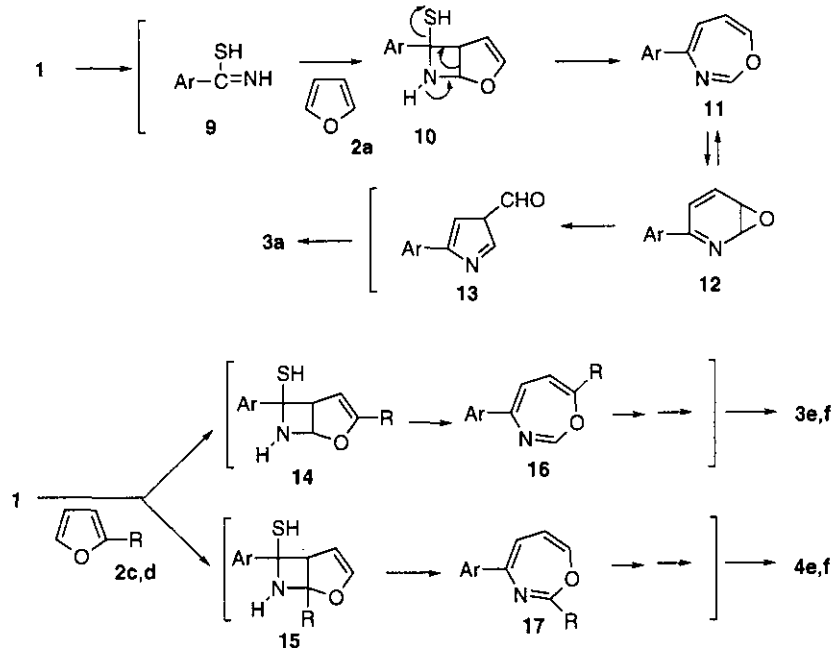


Scheme 1

(**8**) was also readily constructed. Irradiation of furan-2,4-dicarbothioamide (**7**) and 20 eq. of **2a** for 30 h gave exclusively 5-[4-(4-formylpyrrol-2-yl)-2-furyl]pyrrole-3-carbaldehyde (**8**) in 31% yield (Scheme 1).

We already proposed a reaction pathway for the formation of α-arylpyrrole in the photoreaction of benzenecarbothioamide with furan in methanol,[5] by analogy with the known thermal rearrangement from

oxazepine to pyrrole ring.[10] This experiment also indicated that reaction would proceed in several steps involving initial [2 + 2] cycloaddition between the C=N double bond and furan, leading to the aryloxazepine (**11**), which would subsequently rearrange to arylpyrrole as shown in Scheme 2. In the case of 2-substituted furan, from the structural analysis of photoproducts, the reaction seems to proceed *via* formation of two type intermediates (**14**, **15**), leading to two arylpyrroles (**3**, **4**).



Scheme 2

We have developed a new photochemical pyrrole-construction reaction of the thioamide system that promises to have broad application to the synthesis of various pentagonal di- and tri-heterocyclic compounds.

EXPERIMENTAL

All melting points were determined on a Yamato melting point apparatus (model MP-21) and are uncorrected. IR spectra were recorded on a JASCO A-102 spectrophotometer. NMR spectra were taken on JEOL JNM -LA300 and JEOL JNM EX-400 spectrometers. Chemical shifts are reported in ppm (δ) relative to TMS (0.0 ppm) as an internal standard. MS and HRMS spectra were obtained on a Shimadzu GC MS 9100-MK 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 Thioamides (1, 5, 8): Thioamides (**1a**,[6] **1b**,[6] **1c**[11],**5b**[12]) were prepared by the reported procedures. Thioamides (**5a**, **8**) were prepared from the corresponding amides[13] and Lawesson's reagent according to the procedure described in ref. 6. Thioamide (**5c**) was prepared from the corresponding nitrile[14] and hydrogen sulfide according to the procedure described in ref. 15.

Irradiation of Arenecarbothioamides (1) with Furans (2) General Procedure: A solution of **1a** (5 mmol) and **2** (0.1 mol) in methanol (200 mL) was irradiated for 20 h with a 1 kW high-pressure mercury lamp through a Pyrex filter under N_2 at rt. After removal of the solvent *in vacuo*, the residue was chromatographed over a silica gel column (hexane-EtOAc, 3 : 1; v/v).

5-(2-Furyl)pyrrole-3-carbaldehyde (**3a**): mp 190.5-192.0 °C (EtOAc-hexane); IR (nujol): ν_{max} 3300 and 1670 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.52 (1H, m), 6.74 (1H, m), 6.90 (1H, s), 7.42 (1H, s), 7.52 (1H, m), 9.80 (1H, s), 11.35 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 103.5 (d), 105.1 (d), 108.6 (d), 122.3 (s), 129.0 (s), 130.5 (d), 142.5 (s), 143.4 (d), 183.5 (d); MS: m/z 161 (M^+). *Anal.* Calcd for $C_9H_9NO_2$: C, 67.08; H, 4.38; N, 8.69. Found: C, 67.22; H, 4.43; N, 8.81.

5-(2-Thienyl)pyrrole-3-carbaldehyde (**3b**): mp 198.5-199.5 °C (EtOAc); IR (nujol): ν_{max} 3300 and 1670 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.95 (1H, s), 7.02 (1H, m), 7.23 (2H, m), 7.42 (1H, m), 9.75 (1H, s), 11.50 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 103.5 (d), 122.2 (d), 123.3 (d), 126.9 (s), 127.2 (d), 128.0 (d), 129.0 (s), 134.5 (s), 184.9 (d); MS: m/z 177 (M^+). *Anal.* Calcd for C_9H_9NOS: C, 61.00; H, 3.98; N, 7.90. Found: C, 60.92; H, 4.11; N, 7.80.

5-(Pyrrol-2-yl)pyrrole-3-carbaldehyde (**3c**): mp 155 °C (decomp) (EtOAc); IR (nujol): ν_{max} 3300 and 1670 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 7.30 (1H, m), 7.63 (1H, d, *J*=2.4 Hz), 7.86 (1H, s), 8.01 (1H, d, *J*=2.4 Hz), 8.86 (1H, s), 10.90 (1H, s), 12.34 (1H, br s), 13.05 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 99.3 (d), 104.4 (d), 108.4 (d), 118.4 (d), 124.2 (s), 126.9 (s x 2), 129.1 (d), 184.8 (d); MS: m/z 177 (M^+). HRMS m/z Calcd for $C_9H_8N_2O$: 160.0636; Found: 160.0638.

Phenyl 5-(pyrrol-2-yl)pyrrol-3-yl ketone (**3d**): mp 183 °C (decomp) (EtOAc); IR (nujol): ν_{max} 3300 and 1670 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 7.23 (1H, d, *J*=2.4 Hz), 7.29 (2H, m), 7.45 (2H, m), 7.59 (1H, d, *J*=2.4 Hz), 7.62 (2H, m), 7.66 (1H, s), 8.00 (1H, d, *J*=1.5 Hz), 8.13 (1H, s), 12.00 (1H, br s), 12.18 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 99.0 (d), 102.8 (d), 108.0 (d), 117.1 (d), 124.0 (s), 124.5 (d), 125.0(s), 125.5 (s), 126.1 (s), 128.5 (d x 2), 128.9 (d x 2), 130.2 (d), 186.9 (s); MS: m/z 236 (M^+). HRMS m/z Calcd for $C_{15}H_{12}N_2O$: 236.2748; Found: 236.2739.

Methyl 5-(pyrrol-2-yl)pyrrole-3-carboxylate (**3e**): 175-177 °C (EtOAc); IR (nujol): ν_{max} 3300 and 1690 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 3.69 (3H, s), 6.02 (1H, d, *J*=2.4 Hz), 6.32 (1H, s), 6.62 (1H, s), 6.72 (1H, m), 7.36 (1H, m), 11. 01 (1H, br s), 11.58 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 50.6 (q), 102.8 (d), 103.8 (d), 108.2 (d), 115.2 (s), 117.9 (d), 123.1 (d), 124.6 (s), 127.6 (s), 164.6 (s). MS: m/z 190 (M^+). *Anal.* Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63.25; H, 5.43; N, 14.93.

Phenyl 5-(pyrrol-2-yl)pyrrole-3-carboxylate (**3f**): 185-186 °C (EtOAc); IR (nujol): ν_{max} 3300 and 1690 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.02 (1H, d, *J*=2.4 Hz), 6.35 (1H, s), 6.59 (1H, s), 6.72 (2H, m), 7.24 (1H, m), 7.36 (1H, m), 7.50 (2H, m), 7.68 (2H, m), 11. 23 (1H, br s), 11.50 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 101.5 (d), 102.9 (d), 107.9 (d), 118.4 (s), 119.1 (d), 123.4 (d), 123.9 (d), 124.8 (s), 125.7 (d x 2), 127.6 (s), 136.0 (d x 2), 142.1 (s), 167.1 (s). MS: m/z 252 (M^+). HRMS m/z Calcd for $C_{15}H_{12}N_2O_2$: 252.2742; Found: 252.2751.

2-Methoxy-5-(pyrrol-2-yl)pyrrole-3-carbaldehyde (**4e**): mp > 300 °C (decomp) (EtOAc); IR (nujol): ν_{max} 3200 and 1700 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 3.74 (3H, s), 5.67 (1H, d, *J*=2.4 Hz), 6.15 (1H, m), 6.56 (1H, s), 6.91 (1H, d, *J*=1.5 Hz), 9.58 (1H, s), 11.73 (1H, br s), 11.82 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 57.4 (q), 95.9 (d), 107.8 (d), 109.3 (d), 117.4 (s), 119.3 (d), 122.7 (s), 149.0 (s), 172.3 (s), 185.1 (d); MS: m/z 190 (M^+). HRMS m/z Calcd for $C_{10}H_{10}N_2O_2$: 190.0742; Found: 190.0760.

2-Phenoxy-5-(pyrrol-2-yl)pyrrole-3-carbaldehyde (**4f**): mp > 300 °C (decomp) (EtOAc-hexane); IR (nujol): ν_{max} 3200 and 1700 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.01 (1H, d, *J*=2.4 Hz), 6.29 (1H, m), 6.66 (1H, s), 6.94 (1H, d, *J*=1.5 Hz), 7.10 (1H, m), 7.52 (2H, m), 8.29 (2H, m), 9.81 (1H, s), 11.51 (1H, br s), 11.62 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 96.2 (d), 105.3 (d), 108.3 (d), 116.5 (s), 116.9 (d x 2), 119.5 (d), 123.3 (s), 125.5 (d), 131.5 (d x 2), 148.6 (s), 154.2 (s), 171.1 (s), 187.5 (d); MS: m/z 252 (M^+). HRMS m/z Calcd for $C_{15}H_{12}N_2O2$: 252.2742; Found: 252.2732.

5-[5-(4-Formylpyrrol-2-yl)-2-furyl]pyrrole-3-carbaldehyde (**6a**): mp 223-225 °C (EtOAc); IR (nujol): ν_{max} 3300 and 1680 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.56 (2H, d, *J*=3.3 Hz), 6.77 (2H, s), 6.91 (2H, s), 9.76 (2H, s), 11.50 (2H, br s); ^{13}C-NMR (DMSO-d_6): δ 102.4 (d), 108.9 (d), 124.9 (s), 127.5 (d), 128.1 (s), 145.1 (s), 186.0 (d); MS: m/z 254 (M^+). HRMS m/z Calcd for $C_{14}H_{10}N_2O_3$: 254.2466; Found: 254.2469.

5-[5-(4-Formylpyrrol-2-yl)-2-thienyl]pyrrole-3-carbaldehyde (**6b**): mp 208-209 °C (EtOAc); IR (nujol): ν_{max} 3350 and 1690 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.68 (2H, s), 6.79 (2H, s), 6.92 (2H, d, *J*=3.6 Hz), 9.84 (2H, s), 11.65 (2H, br s); ^{13}C-NMR (DMSO-d_6): δ 102.6 (d), 122.8 (d), 125.3 (s), 127.1 (d), 128.9 (s), 135.9 (s), 185.2 (d); MS: m/z 270 (M^+). HRMS m/z Calcd for $C_{14}H_{10}N_2O_3$: 270.3138; Found:

270.3146

5-[5-(4-Formylpyrrol-2-yl)pyrrol-2-yl]pyrrole-3-carbaldehyde (**6c**): mp 196-198 °C (EtOAc); IR (nujol): ν_{max} 3400 and 1680 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.58 (2H, m), 6.68 (2H, s), 6.79 (2H, s), 9.88 (2H, s), 11.30 (2H, br s); ^{13}C-NMR (DMSO-d_6): δ 105.2 (d), 121.4 (d), 124.9 (s), 128.5 (d), 128.9 (s), 137.1 (s), 187.4 (d); MS: m/z 253 (M^+). HRMS m/z Calcd for $C_{14}H_{11}N_3O_2$: 253.2619; Found: 253.2611.

5-[4-(4-Formylpyrrol-2-yl)-2-furyl]pyrrole-3-carbaldehyde (**8**): mp 201-202 °C (EtOAc); IR (nujol): ν_{max} 3350 and 1680 cm^{-1}; ^{1}H-NMR (DMSO-d_6): δ 6.52 (1H, s), 6.77 (1H, s), 6.91 (1H, s), 7.25 (1H, s), 7.32 (1H, s), 7.39 (1H, s), 9.85 (1H, s), 9.62 (1H, s), 11.30 (1H, br s), 11.65 (1H, br s); ^{13}C-NMR (DMSO-d_6): δ 104.5 (d), 105.8 (d), 108.9 (d), 118.2 (s), 119.3 (s), 120.3 (s), 124.9 (s), 124.5 (d), 125.9 (d), 128.1 (s),145.1 (s), 148.5 (d), 184.3 (d), 186.0 (d); MS: m/z 254 (M^+). HRMS m/z Calcd for $C_{14}H_{10}N_2O_3$: 254.2466; Found: 254.2455.

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