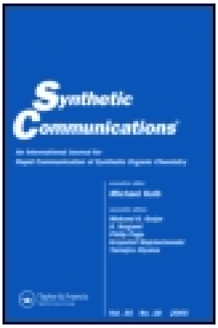

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Photoreaction of Benzenecarbothioamide with Aldehydes. Facile Synthesis of Tetracyclic Imidazoles.[1])

Kazuaki Oda [a], Masayuki Sakai [a], Hisao Tsujita [a] & Minoru Machida [a]
[a] Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido, 061-02, Japan

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PHOTOREACTION OF BENZENECARBOTHIOAMIDE WITH ALDEHYDES.

FACILE SYNTHESIS OF TETRACYCLIC IMIDAZOLES.¹⁾

Kazuaki Oda,* Masayuki Sakai, Hisao Tsujita and Minoru Machida

Faculty of Pharmaceutical Sciences, Health Sciences University of Hokkaido,
Ishikari-Tobetsu, Hokkaido 061-02, Japan

Abstract: *Photoreaction of benzenecarbothioamide with various aldehydes in benzene solution gave 2-substituted phenanthroimidazoles.*

Since imidazoles have a key role in a variety of pharmaceuticals and are found in many biologically active natural products,²⁾ their synthesis has received considerable attention. Although numerous synthetic routes to imidazole systems are well known,³⁾ little is known about the general synthetic method to multicyclic imidazole system such as phenanthroimidazole derivatives, which are extensively investigated on biological activity⁴⁾ and used as fluorophore of derivatization reagents in HPLC.⁵⁾ As a part of a continuing study on the photochemistry of arenecarbothioamide systems,⁶⁻⁸⁾ a construction of the tetracyclic imidazole system

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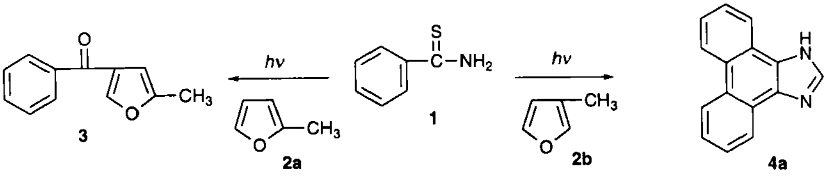
*To whom correspondence should be addressed.

was found. In this paper we report the facile synthesis of 1*H*-phenanthro[9,10-*d*]imidazole derivatives by photoreaction of benzenecarbothioamide with aldehydes.

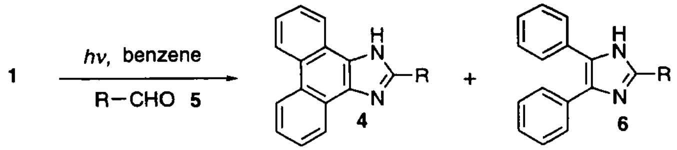
As has already been reported, upon irradiation of a benzene solution of benzenecarbothioamide (**1**) and 2-methylfuran (**2a**), 3-benzoylfuran derivative (**3**) was obtained in 67 % yield.[8] However, in the reaction of **1** with 3-methylfuran (**2b**), a product of an unpredictable type, 1*H*-phenanthro[9,10-*d*]imidazole (**4a**) was obtained in 18 % yield, and no benzoylated product was detected.



Scheme 1

This finding suggested a possibility of synthesis of tetracyclic imidazoles. So it was assumed that the **4a** was consisted of two molecules of **1** and one carbon unit. From the fact that photodecomposition of **2b** involves generation of carbon monoxide,[9] we speculated that one carbon atom in **4a** is derived from formaldehyde. In order to investigate whether aldehyde participates or not in imidazole formation, irradiation of **1** and simple aldehydes (**5a-e**) in benzene solution was examined. The results are listed in Table 1. Irradiation of **1** and three equivalents of formaldehyde (**5a**) for 20 hr gave **4a** and 4,5-diphenylimidazole (**6a**) in 23 and 6 % yields, respectively. Similarly, with acetaldehyde (**5b**), cyclohexanecarbaldehyde (**5c**) and benzaldehyde (**5d**), phenanthroimidazole derivatives (**4b-d**) were obtained in 8 - 19 % yields accompanied by 2-substituted 4,5-diphenylimidazole derivatives (**6b-d**) in 14 - 24 % yields, respectively.

Table 1. Photoreaction of 1 with 5

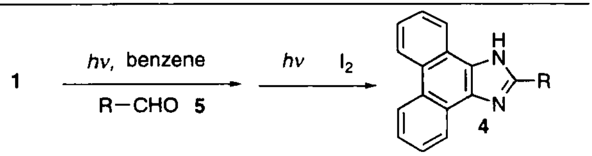


5a: R = H	**4a** 23 %	**6a** 6 %
5b: R = CH_3	**4b** 19 %	**6b** 14 %
5c: R = cyclohexyl	**4c** 16 %	**6c** 17 %
5d: R = phenyl	**4d** 8 %	**6d** 24 %

Next, we tried photochemical conversion of the 4,5-diphenylimidazole derivatives (**6a-d**) into phenanthroimidazole derivatives (**4a-d**) in the presence of iodine.[10] Photoproduct **6a** was photochemically converted to **4a** in quantitative yield. In a similar manner, **6b-d** was easily converted into 2-substituted phenanthroimidazole derivatives (**4b-d**).

In order to obtain efficiently 2-substituted phenanthroimidazole without isolating the 4,5-diphenylimidazole, based on the above results, one pot photoreaction was carried out. After irradiation for 20 hr, iodine was added to the photolytic solution, which was further irradiated for 2 hr and chromatographed. Similarly, photoreactions of **1** with other aldehydes (**5e-g**) were performed under similar conditions. As expected, 2-substituted phenanthroimidazole derivatives (**4a-g**) were obtained in moderate yields (35 - 52 %) as sole products . The results are listed in Table 2. The spectral and physical data of **4a** (decomp. 222 °C; lit.,[5] decomp. 220 °C), **4b** (mp. 255-257 °C; lit.,[10] 258 °C), **4d** (mp. > 300 °C; lit.,[11] 312-314 °C), **4e** (mp. 219-220 °C; lit.,[5] 218 °C), **4f** (mp. 253.5-255 °C; lit.,[12] 254-255 °C), **4g** (mp. 279-283 °C; lit.,[11] 282-284 °C), **6a** (mp.

Table 2. Photoreaction of **1** with **5** in the presence of iodine



5a: R = H	**4a** 42 %
5b: R = CH_3	**4b** 38 %
5c: R = cyclohexyl	**4c** 40 %
5d: R = phenyl	**4d** 52 %
5e: R = $CH_2(CH_2)_4CH_3$	**4e** 35 %
5f: R = 4-pyridyl	**4f** 47 %
5g: R =4-methylphenyl	**4g** 42 %

231.5-233 °C; lit.,[13] 233-234 °C), **6b** (mp. 244-246 °C; lit.,[13] 242-243.5 °C) and **6d** (mp. 276-278 °C; lit.,[5] 275-277 °C) were identical with those reported. The structures of other photoproducts (**4c**, **6c**) were also determined on the basis of the spectral and analytical data.

The present photoreaction would provide a convenient one step synthesis of phenanthroimidazole derivatives, and is of both mechanistic and synthetic interest.

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 EX-400 spectrometer. Chemical shifts are reported in ppm (δ) relative to TMS (0.0 ppm) as an internal standard. The abbreviations used are as follows: s, singlet; d, doublet; m, multiplet. Mass spectra (MS) were obtained on a JEOL JMS-QH-100 gas chromatograph-mass spectrometer. Preparative irradiations were conducted by using a 1kW 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 reaction vessel. Column chromatography was conducted using silica gel (Merck, Kieselgel 60, 70-230 mesh)

Irradiation of benzenecarbothioamide (1) with 3-methylfuran (2b)

A mixture of **1** (5 mmol) and **2b** (15 mmol) in benzene (200 ml) was irradiated for 20 hr 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 on silica gel using a mixture of n-hexane-ethyl acetate (1 : 2; v/v).

Irradiation of benzenecarbothioamide (1) with aldehydes (5): General Procedure

A mixture of **1** (5 mmol) and **5** (15 mmol) in benzene (200 ml) was irradiated for 20 hr 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 on silica gel using a mixture of n-hexane-ethyl acetate (1 : 2; v/v). The results are listed in Table 1.

4c: m.p. 260-264°C; IR (nujol) 3000 cm^{-1} (NH); ^{1}H-NMR ($CDCl_3$) δ 1.27-2.28 (11H, m), 7.62 (6H, m, aromatic H), 8.34 (1H, br s, NH), 8.73 (2H, d, J = 8.3 Hz, aromatic H); ^{13}C-NMR ($CDCl_3$) δ 25.9 (t), 26.1 (t x 2), 32.4 (t x 2), 38.8 (d), 123.7 (d x 2), 124.9 (s x 4), 126.7 (s x 2), 126.9 (d x 2), 128.1 (s x 4), 156.1 (s); MS (m/z) 300 (M^+); *Anal.* Calcd for $C_{21}H_{20}N_2$: C, 83.96; H, 6.71; N, 9.33. Found: C, 83.78; H, 6.89; N, 9.33.

6c: m.p. 240-242°C; IR (nujol) 3300 cm^{-1} (NH); ^{1}H-NMR ($CDCl_3$) δ 1.27-1.93 (11H, m), 7.22-7.39 (10H, m, aromatic H), 7.56 (1H, br s, NH); ^{13}C-NMR ($CDCl_3$) δ 25.8 (t), 26.1 (t x 2), 32.0 (t x 2), 37.8 (d), 127.1 (s x 2), 127.3

(d x2), 127.8 (d x 4), 128.6 (d x 4), 128.7 (s x 2), 152.4 (s); MS (m/z) 302 (M^+); *Anal.* Calcd for $C_{21}H_{22}N_2$: C, 83.39; H, 7.34; N, 9.27. Found: C, 83.30; H, 7.21; N, 9.49.

Irradiation of benzenecarbothioamide (1) with aldehydes (5) in the presence of iodine: General Procedure

A mixture of **1** (6 mmol) and **5** (15 mmol) in benzene (200 ml) was irradiated for 20 hr with a 1 kW high-pressure mercury lamp through a Pyrex filter under N_2 at room temperature. After irradiation, 0.2 g of iodine was added to the photolytic solution, which was further irradiated for 2 h. The solvent was removed *in vacuo* and the residue was chromatographed over silica gel using a mixture of n-hexane-ethyl acetate (1 : 2; v/v). The results are listed in Tables 2.

Acknowledgement

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