

## A Novel Photochemical Reaction of 4-Bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one

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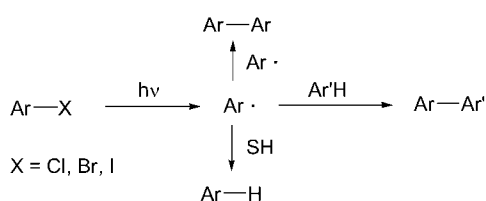
UV-Irradiation of 4-bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one (**1**) in the presence of various aromatic hydrocarbons gave different types of photoproducts depending on the nature of the hydrocarbons via an electron-transfer mechanism. In the presence of naphthalene or phenanthrene a photochemical homocoupling reaction of **1** occurred to form **2** or **2** and **3**, respectively.

**Keywords**    photocoupling, pyrazolone, exciplex, electron-transfer mechanism

### Introduction

Aryl halides are well known to undergo a photocoupling reaction with aromatic hydrocarbons (Ar'H) leading to hetero-biaryls (Ar—Ar') via the initial formation of aryl radical intermediates (Ar·), which are reduced to the parent hydrocarbon (ArH) in the presence of a hydrogen donor (SH), but the formation of homocoupling biaryls (Ar—Ar) is a very minor path (Scheme 1).<sup>1</sup>

#### Scheme 1

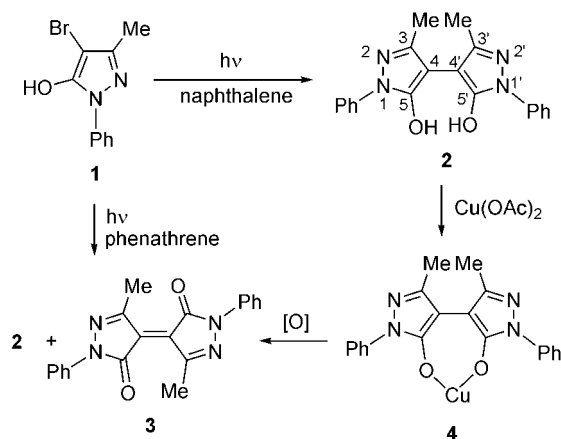


There are also numbers of reports from our laboratories on the synthesis of biaryl-type of compounds using the photocoupling of haloarenes or halo-heteroarenes with heteroarenes or arenes<sup>2</sup> and on the applications of this method to the preparation of fluorescent analogs of quaterphenyl and 5- and 6-substituted pyrimidines as DNA probes.<sup>3</sup> Only an exceptional case was found in the photoreaction of 5-bromo-1,3-dimethyluracil in the presence of 9-methylantracene to give a homocoupling product (Ar—Ar), 5,5'-bis(1,3-dimethyluracil) as the major product.<sup>3e</sup>

As a continuation of our interest in the chemistry<sup>4-6</sup> of pyrazolones, we have investigated the photochemical reaction of 4-bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one (**1**) in the presence of various aromatic hydrocarbons. It was found that the reaction showed different features for the halo-heterocyclic compounds

which gave heterocoupling biaryls,<sup>2,3</sup> *i.e.* in the presence of a particular aromatic hydrocarbon the major products were homocoupled product **2** [4,4'-bis(3-methyl-1-phenyl-5-oxo-4,5-dihydro-pyrazol-4-yl)] and its dehydrogenated product **3** [4-(3'-methyl-1'-phenyl-5'-hydro-pyrazol-5'-on-4'-ylidene)-3-methyl-1-phenyl-5-hydro-pyrazol-5-one] as a rare case (Scheme 2).

#### Scheme 2



### Results and discussion

The photoreactions were conducted by irradiating a solution of a mixture of **1** (PyHBr) (1 mmol) and an arene (2 mmol) in acetonitrile (25 mL) with a 300 W high-pressure mercury lamp for 24 h under nitrogen atmosphere at room temperature. In the presence of naphthalene, the homocoupled product **2** was found to be the major product (64%), while in the presence of phenanthrene a mixture of **2** (29%) and its dehydrogenated product **3** (41%) was obtained. On the other hand,

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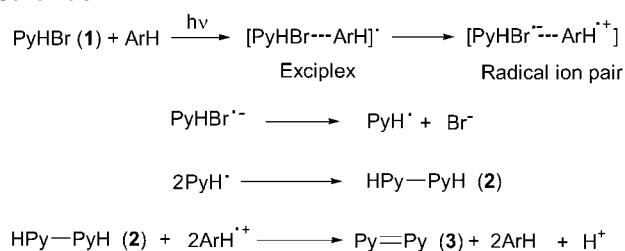
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in the presence of the equimolar amount of anthracene under the similar irradiation conditions the known photodimer of anthracene was obtained as the sole product and no reaction similar to the above was observed. It should be noted that in the presence or absence of a certain aromatic or heteroaromatic compound, such as benzene, acenaphthylene and indole (**1** : ArH = 1 : 2), **1** was mostly recovered under the similar irradiation conditions.

The structures of **2** and **3** were deduced on the basis of their microanalytical and spectral data. Among them the broad IR band of **2** at around  $2650\text{ cm}^{-1}$  was assigned to the strongly hydrogen-bonded enolic hydroxyl due to a cooperative proton transfer.<sup>7,8</sup> The presence of this acidic proton in **2** was evident from the formation of its cupric salt **4**. In the  $^1\text{H}$  NMR spectrum of the dehydrogenated product **3**, a peak of methyl protons at  $\delta$  2.69 appeared with a highly down-field shift as compared to that of **2** at  $\delta$  2.14. The result indicates that **3** has (*E*)-stereochemistry in which closely located methyl and carbonyl groups are coplanar.<sup>9</sup> Bispyrazolone **2** exhibited an autooxidisable property. Treatment of **2** with  $\text{Cu}(\text{OAc})_2$  in ethanol precipitated its copper salt **4** as a brown solid which was gradually converted into **3** in ethanol solution under air atmosphere.

The formation of homocoupled products **2** and **3** from the heteroaromatic bromide **1** provides a novel synthetic route to biaryls from aryl halide which is also interesting from the mechanistic point of view. It is generally accepted as Scheme 1 that the aryl radical resulted from the homolytic cleavage of an aryl halide. For the present homocoupling reaction of **1**, such a simple radical cleavage mechanism is not applicable, because no carbon-halogen bond cleavage was observed in the absence of an aromatic hydrocarbon or even in the presence of a certain aromatic hydrocarbon such as benzene, acenaphthylene or indole under the UV-irradiation conditions. Therefore, the electron-transfer mechanism via an exciplex  $[\text{PyHBr}\cdots\text{ArH}]^*$  and subsequent radical ion pair  $[\text{PyHBr}^{\cdot-}\cdots\text{ArH}^{\cdot+}]$  as elucidated in Scheme 3 might be applicable in the present case, as has been suggested for the formation of a homocoupled product [5,5'-bis(1,3-dimethyluracil)] in the previously reported photoreaction of 5-bromo-1,3-dimethyluracil in the presence of 9-methyl-anthracene.<sup>3d</sup> The formation of the dehydrogenated product **3** is interpreted by the dehydrogenation of **2** with the arene cation radicals (Scheme 3).

### Scheme 3



In order to contribute to the understanding of this mechanism, we examined the effect of the molar ratio of the substrates on the product ratio (**2/3**) in the homocoupling reaction of **1** in the presence of phenanthrene. The results in Table 1 indicated that the variation of the molar ratio of the reaction compounds gave no effect on the product ratio and the results did not imply any definite features of the present reaction.

**Table 1** Photoreaction of **1** with phenanthrene in different ratios in acetonitrile

<b>1</b> : phenanthrene	Yield/% of <b>2</b>	Yield/% of <b>3</b>	Ratio of <b>2/3</b>
1 : 3	27.2	40.0	0.68
1 : 2	28.9	40.7	0.71
1 : 1	28.1	41.0	0.69
1 : 0.5	25.1	36.3	0.69
1 : 0	0	0	—

In conclusion, we have found a novel photochemical homocoupling reaction of **1** leading to **2** or **2** and **3** in the presence of naphthalene or phenanthrene which is rare in the photoreaction of aryl and heteroaryl halides. The further investigation on the scope and the nature of this novel photoreaction is being undergone in this laboratory.

## Experimental

### General procedure

All melting points were uncorrected. NMR spectra were recorded on a Bruker AC-P200 spectrometer using internal tetramethylsilane ( $\text{Me}_4\text{Si}$ ) as the reference. Mass spectra were determined with a 7070E-HE mass spectrometer. Elemental analyses were carried out on a Yanaco CHN CORDER MT-3 elemental analyzer. IR spectra were recorded on a Bio-Rad FTS 135 spectrometer. Acetonitrile was dried over  $\text{CaH}_2$  and distilled before use.

### Photoreaction of 4-bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one (**1**) in the presence of naphthalene

A solution of **1** (0.25 g, 1 mmol) and naphthalene (0.25 g, 2 mmol) in acetonitrile (25 mL) was deoxygenated by bubbling with nitrogen and irradiated with a 300 W high-pressure mercury lamp for 24 h at room temperature. Precipitated white crystals were collected by filtration, washed with acetonitrile and recrystallized from methanol-acetonitrile to give the homocoupled biaryl **2** (0.11 g, 64% yield) as colorless plates. m.p.  $311\text{--}312\text{ }^\circ\text{C}$ ;  $^1\text{H}$  NMR ( $\text{DMSO-}d_6$ )  $\delta$ : 2.14 (s, 6H, 2CH<sub>3</sub>), 3.41 (brs, 2H, 2OH), 7.20—7.80 (m, 10H);  $^{13}\text{C}$  NMR ( $\text{DMSO-}d_6$ )  $\delta$ : 11.51 (CH<sub>3</sub>), 99.42 (4-C), 124.66 (Ph), 128.02 (Ph), 128.18 (Ph), 135.29 (Ph), 149.63 (3-C), 158.91 (5-C); IR (KBr)  $\nu$ : 3330, 2650 (br), 1560, 1497, 755  $\text{cm}^{-1}$ ; MS (70 eV)  $m/z$  (%): 347 ( $\text{M}^+ + 1$ , 10.7), 346 ( $\text{M}^+$ , 45.7), 315 (2.2), 241 (4.4), 226 (4.0),

213 (11.4), 173 (12.8), 119 (3.4), 105 (8.7), 77 (100), 40 (26.1). Anal. calcd for  $C_{20}H_{18}N_4O_2$ : C 69.36, H 5.20, N 16.18; found C 69.17, H 5.14, N 16.26.

#### Photoreaction of 4-bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one (1) in the presence of phenanthrene

A solution of **1** (0.25 g, 1 mmol) and phenanthrene (0.36 g, 2 mmol) in acetonitrile (25 mL) was degassed and irradiated as above. Evaporation of the reaction mixture left a mixture of white and dark blue solid. The solid was treated with hot acetonitrile (50 mL) and insoluble **2** (48 mg) was collected by filtration, m.p. 311—312 °C. The cooling of the filtrate gave **3** (62 mg) as dark blue needles, m.p. 254 °C (dec.). The combined mother liquors were concentrated and the residue was applied to a silica gel column chromatography with 1 : 3 acetone-petroleum ether (b.p. 60—90 °C) to give another crop of **2** (2.5 mg) and **3** (8.4 mg) and recovered phenanthrene 353 mg (99.2%). The total yields were 29% for **2** and 41% for 4-(3'-methyl-1'-phenyl-5'-hydro-pyrazol-5'-on-4'-ylidene)-3-methyl-1-phenyl-5-hydro-pyrazol-5-one (**3**). Dark blue needles (from acetonitrile), m.p. 254 °C;  $^1H$  NMR (DMSO- $d_6$ )  $\delta$ : 2.69 (s, 6H, 3CH<sub>3</sub>), 7.24—7.57 (m, 6H, ArH), 7.61—7.93 (m, 4H, ArH);  $^{13}C$  NMR (DMSO- $d_6$ )  $\delta$ : 12.10 (CH<sub>3</sub>), 120.43 (Ph), 124.05 (Ph), 128.80 (Ph), 139.86 (4-C), 140.26 (Ph), 147.52 (3-C), 159.89 (5-C); IR (KBr)  $\nu$ : 3060, 2990, 1694, 1595, 1490, 1367, 1287, 1124, 932, 759  $cm^{-1}$ ; MS (70 eV)  $m/z$  (%): 345 ( $M^+ + 1$ , 7.3), 344 ( $M^+$ , 28.5), 316 (5.0), 315 (18.0), 239 (3.3), 211 (6.4), 119 (2.7), 105 (4.1), 78 (11.0), 77 (100), 40 (7.8). Anal. calcd for  $C_{20}H_{16}N_4O_2$ : C 69.77, H 4.65, N 16.28; found C 69.39, H 4.49, N 15.98.

The similar photoreaction was conducted in the presence of different amounts of phenanthrene. The results are listed in Table 1.

#### Photoreaction of 4-bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one (1) in the presence of anthracene

A saturated solution of anthracene (2 mmol) in acetonitrile (25 mL) containing **1** (0.25 g, 1 mmol) was degassed and irradiated as above. Colorless crystals precipitated during irradiation were identified to be the photodimer of anthracene, m.p. 249—250 °C. The starting material **1** was recovered unchanged and no other product was detected in the irradiated mixture.

#### Photoreaction of 4-bromo-3-methyl-1-phenyl-4,5-dihydro-pyrazol-5-one (1) in the presence of various aromatic compounds

A solution of **1** (0.25 g, 1 mmol) in acetonitrile (25 mL) containing acenaphthylene (0.60 g, 4 mmol) or indole (0.23 g, 2 mmol) or benzene (0.5 mL, a large excess) was degassed and irradiated as above. No reaction product was detected by TLC analysis of the irradiated mixture.

#### Control experiments

**Irradiation of 1 in the absence of an aromatic compound** A solution of **1** (0.5 mmol) in acetonitrile (15 mL) was degassed and irradiated as above. No reaction product was detected by TLC analysis.

**Thermal reaction of 1** A solution of **1** (0.25 g, 1 mmol) in acetonitrile (25 mL) was refluxed under nitrogen atmosphere for 6 h. TLC analysis of the heated solution showed that no reaction occurred.

**Copper(II) salt (4) of 2** A solution of  $Cu(OAc)_2 \cdot H_2O$  (0.10 g, 0.5 mmol) in ethanol (15 mL) was added dropwise to an ethanol solution of **2** (0.17 g, 0.5 mmol) under nitrogen with stirring. A brown precipitate formed instantly. After stirring for 5 min, the precipitate was separated by centrifugation, washed with 95% ethanol (30 mL  $\times$  2) and ethanol (30 mL  $\times$  2) successively and dried *in vacuo* to give Cu(II) salt (**4**) as a brown solid (196 mg, 96.1%). m.p. 250 °C (dec.); IR (KBr)  $\nu$ : 3054, 2990, 1596, 1562, 1498, 751  $cm^{-1}$ . Anal. calcd for  $C_{20}H_{16}N_4O_2Cu$ : C 58.89, H 3.94, N 13.74, Cu 15.58; found C 59.23, H 3.77, N 13.38, Cu 15.17.

Similar treatment of **2** with a solution of other transition metal salts, such as  $Ni(OAc)_2 \cdot 4H_2O$ ,  $Mn(OAc)_2 \cdot 4H_2O$  and  $Cr(OAc)_2 \cdot H_2O$  gave no precipitation of their metal complex.

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