Synthesis and Fluorescent Properties of 2-Arylamino-5-(3-aryl-1-phenyl-pyrazol-4-yl)-1,3,4-thiadiazoles

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A series of novel pyrazolyl-substituted 1,3,4-thiadiazole derivatives (**6a**-**6d**, **7a**-**7d**, **8a**-**8d**) were prepared by cyclization of the intermediate 3-aryl-l-phenyl-pyrazol-4-ylformaldehyde 4′-phenylthiosemicarbazones with 0.5 M ferric chloride solution. The structures of the new compounds were confirmed by IR, ^{1}H NMR and elemental analysis. Simultaneously, the compounds were detected by fluorescence spectrophotometer and had preferable fluorescence activity.

Keywords: 4-Formylpyrazole; 1,3,4-Thiadiazole; Fluorescent property.

INTRODUCTION

Several pyrazole derivatives exhibit anti-inflammatory, antimicrobial, analgesic and antipyretic activities.[1-4] Various substituted thiadiazoles also exhibit biological behavior.[5-7] A large number of 1,3,4-thiadiazoles have become very useful compounds in many fields of technology. Some of the technological applications involve photographic materials,[8] lubricating compositions,[9] optically active liquid crystals, light-emitting materials[10] and many others. In addition, fluorescent detection is of paramount importance to biological studies.[11,12] The sensitivity of fluorescence techniques has reached an extremely high level, similar to radioactive methods, and can even provide information on the dynamic structure of dyebound biomolecules. Therefore, interest in the synthesis of pyrazole with a thiadiazolyl group substituted at a suitable position by a convenient method is significant. In view of this, some novel 1,3,4-thiadiazoles containing pyrazole ring were synthesized by the reaction of 3-aryl-l-phenyl-pyrazol-4-ylformaldehyde 4′-phenylthiosemicarbazones with 0.5 M ferric chloride solution (Scheme I).

RESULTS AND DISCUSSION

Thiosemicarbazones exhibit various biological activities and are extensively applied in medicine-particularly in the treatment of tuberculosis.[13] Numerous compounds with a thiosemicarbazone moiety also exhibit biological activity.[14] Accordingly, 3-aryl-l-phenyl-pyrazol-4-ylformaldehyde 4′-phenylthiosemicarbazones **3a**-**3d**, **4a**-**4d**, and **5a**-**5d** were synthesized in good yields by the reactions of 3-aryl-1-phenyl-4-formylpyrazole **1a**-**1c** with 4′-phenylthiosemicarbazide **2a**-**2d**.

In this study, we found that the temperature of the reaction has a great impact on the level of yield. The treatment of 3-aryl-l-phenyl-pyrazol-4-ylformaldehyde 4′-phenylthiosemicarbazones (**3b**-**5b**) with ferric chloride in ethanol solution, following by heating under 70 °C in an oil bath for about 2 h, produced the desired products **6b**-**8b** with favorable yields (Table 1), while other target compounds were synthesized under 80 °C.

The IR spectrum of compounds **6a**-**6d**, **7a**-**7d** and **8a**-**8d** showed broad bands at 3400-3200 cm^{-1}, assigned to their NH. The strong bands appearing at around 1620 cm^{-1} were attributed to absorption of C=C in pyrazole ring. The appearance of the absorption at 1450-1600 cm^{-1} was ascribed to benzene skeleton vibration. The signals at 697 cm^{-1} were identified as C–S–C in thiadiazole ring.

The ^{1}H NMR of compounds **6a**-**6d**, **7a**-**7d**, **8a**-**8d** in $CDCl_3$ showed a few single peaks at δ 8.80-10.60 due to the proton of N–H, multiple peaks at δ 6.90-7.90 ascribable to aromeric protons and peaks at δ 8.39-8.55 assignable to methylidene proton of the pyrazole group owing to the deshielding effect of the larger conjugated system formed by cycle-pyrazole and cycle-thiadiazole.

Solid-state fluorescence spectrum of compounds **6a**-**6d**, **7a**-**7d** and **8a**-**8d** were determined with solid powder on a quartzround plate with excitation and emission slits of 2.5/2.5 nm by spectrophotometry. The optimum excitation

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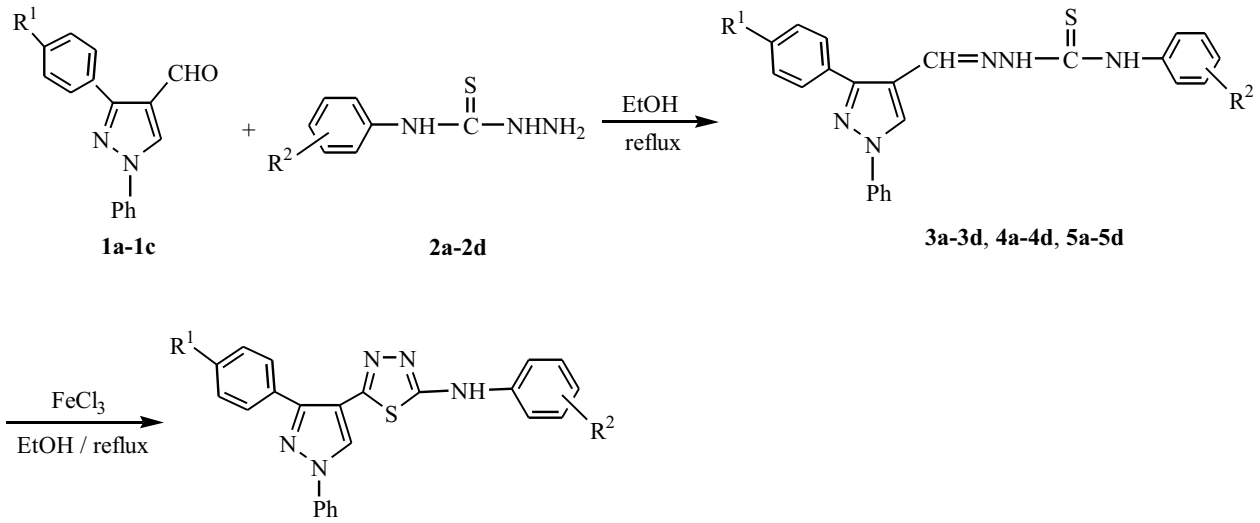
Scheme I



2a-2d: **a**: R^2 = H; **b**: R^2 = 2-CH_3; **c**: R^2 = 4-CH_3; **d**: R^2 = 4-Cl;
1a, **3a-3d**, **6a-6d**: R^1 = H; **a**: R^2 = H; **b**: R^2 = 2-CH_3; **c**: R^2 = 4-CH_3; **d**: R^2 = 4-Cl;
1b, **4a-4d**, **7a-7d**: R^1 = OCH_3; **a**: R^2 = H; **b**: R^2 = 2-CH_3; **c**: R^2 = 4-CH_3; **d**: R^2 = 4-Cl;
1c, **5a-5d**, **8a-8d**: R^1 = Br; **a**: R^2 = H; **b**: R^2 = 2-CH_3; **c**: R^2 = 4-CH_3; **d**: R^2 = 4-Cl.

wavelength of compounds **6**, **7** and **8** was 350 nm. The fluorescence spectrum of compounds **6**, **7** and **8** excited at optimum excitation wavelength of each compound, respectively; at the same time, the emission wavelengths of compounds **6**, **7** and **8** were measured by the optimum excitation wavelength. The emission wavelengths of compounds **6a-6d** were 418, 417, 420, 429 nm; meanwhile, the emission wavelengths of **7a-7d** were 427, 360, 422, 425 nm, and the emission wavelengths of **8a-8d** were 433, 433, 428, 424 nm. As shown in Fig. 1. These fluorescence spectrum corresponded to the transitions of n→π* and π→π*. From the Fig. 1, we know the fluorescence intensity of compounds **6a**, **6b**, **6c** and **8a** is very strong. Compounds **7c**, **7d** and **8d** also display relatively good fluorescence activity. In summary, most of the target compounds will present fluorescence in the visible region. Thus, they could be of potential application for the fabrication of organic light-emitting diodes.

EXPERIMENT

General Method

The ^{1}H NMR spectra were recorded on an Inova-400 (using TMS as internal standard, $CDCl_3$ as solvent). The IR spectra were obtained on a Bruker Equinox 55 FT-IR appa-

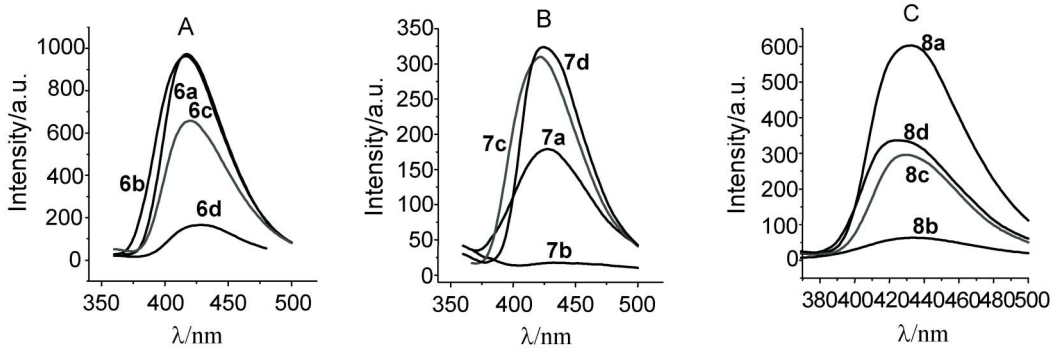


Fig. 1. Fluorescence spectra of compounds **6a-6d** (A), **7a-7d** (B) and **8a-8d** (C).

Table 1. Physical data and elemental analysis of compounds

Compd.	m.p./°C	Yield/%	Formula	Analysis found (calcd.) %		
				C	H	N
6a	223-225	65	$C_{23}H_{17}N_5S$	69.97 (69.85)	4..31 (4.33)	17.76 (17.71)
6b*	194-195	57	$C_{24}H_{19}N_5S$	70.26 (70.39)	4.69 (4.68)	17.15 (17.10)
6c	228-230	68	$C_{24}H_{19}N_5S$	70.27 (70.39)	4.70 (4.68)	17.12 (17.10)
6d	250-251	63	$C_{23}H_{16}ClN_5S$	64.31 (64.25)	3.74 (3.75)	16.33 (16.29)
7a	238-240	71	$C_{24}H_{19}N_5OS$	67.61 (67.74)	4.51 (4.50)	16.50 (16.46)
7b*	> 280	65	$C_{25}H_{21}N_5OS$	68.42 (68.32)	4.80 (4.82)	15.96 (15.93)
7c	219-220	72	$C_{25}H_{21}N_5OS$	68.44 (68.32)	4.81 (4.82)	15.94 (15.93)
7d	273-274	77	$C_{24}H_{18}ClN_5OS$	62.53 (62.67)	3.96 (3.94)	15.27 (15.23)
8a	271-273	62	$C_{23}H_{16}BrN_5S$	58.30 (58.23)	3.41 (3.40)	14.71 (14.76)
8b*	> 280	49	$C_{24}H_{18}BrN_5S$	59.13 (59.02)	3.73 (3.71)	14.38 (14.34)
8c	> 280	71	$C_{24}H_{18}BrN_5S$	59.08 (59.02)	3.70 (3.71)	14.32 (14.34)
8d	275-276	60	$C_{23}H_{15}lBrClN_5S$	54.21 (54.29)	2.99 (2.97)	13.81 (13.76)

* The compounds **6b**-**8b** were synthesized under 70 °C

ratus by a pressed KBr pellet. Elemental analyses were performed on a Thermo Flash EA-1112 analyzer. Melting points were taken on a Yanaco MP-S3 micromelting point apparatus. Corrected fluorescence spectra were taken on a Hitachi F-4500 fluorescence spectrophotometer. All reagents were analytical grade chemicals, which could not be utilized before not being disposed, except for special introduction. The boiling point range of petroleum ether was 60-90 °C. The TLC was performed by GF_{254} and 0.5% CMC. Detection made use of UV light; the mobile phase was petroleum ether and ethyl acetate (1:3, *V*/*V*).

1. Preparation of 3-aryl-1-phenyl-4-formylpyrazole (1a-1c) according to the literature[15]

2. Synthesis of 3-aryl-l-phenyl-pyrazol-4-ylformaldehyde 4′-phenylthiosemicarbazones (3a-3d, 4a-4d, 5a-5d)[16]

To a suspension of 3-aryl-l-phenyl-4-formylpyrazoles (**1a-1c)** (3 mmol) in ethanol (20 mL) was added an equivalent amount of N^4-substituted thiosemicarbazide (**2a**-**2d**). The reaction mixture was heated under reflux for

Table 2. ^{1}H NMR, IR data of compounds

Compd.	^{1}H NMR ($CDCl_3$) δ	IR (KBr) ν/cm^{-1}
6a	10.30 (s, 1H, NH), 8.50 (s, 1H, pyrazole-H), 7.10-7.90 (m, 15H, ArH)	3263, 1625, 1600, 1566, 1455
6b	10.06 (s, 1H, NH), 8.46 (s, 1H, pyrazole-H), 7.00-7.90 (m, 14H, ArH), 2.34 (s, 3H, CH_3)	3321, 1617, 1605, 1584, 1470
6c	9.86 (s, 1H, NH), 8.43 (s, 1H, pyrazole-H), 6.90-7.90 (m, 14H, ArH), 2.29 (s, 3H, CH_3)	3362, 1612, 1603, 1573, 1452
6d	10.01 (s, 1H, NH), 8.39 (s, 1H, pyrazole-H), 6.90-7.90 (m, 14H, ArH)	3246, 1619, 1599, 1563, 1450
7a	10.42 (s, 1H, NH), 8.48 (1H, pyrazole-H), 7.00-7.90 (m, 14H, ArH), 3.85 (s, 3H, OCH_3)	3328, 1624, 1537, 1608, 1437
7b	9.98 (s, 1H, NH), 8.42 (s, 1H, pyrazole-H), 6.90-7.90 (m, 13H, ArH), 3.85 (s, 3H, OCH_3), 2.22 (s, 3H, CH_3)	3357, 1619, 1564, 1612, 1458
7c	10.02 (s, 1H, NH), 8.44 (s, 1H, pyrazole-H), 6.90-7.90 (m, 13H, ArH), 3.83 (s, 3H, OCH_3), 2.23 (s, 3H, CH_3)	3343, 1613, 1595, 1561, 1437
7d	10.51 (s, 1H, NH), 8.45 (s, 1H, pyrazole-H), 7.00-7.90 (m, 13H, ArH), 3.79 (s, 3H, OCH_3)	3351, 1607, 1556, 1601, 1452
8a	8.82 (s, 1H, NH), 8.43 (s, 1H, pyrazole-H), 7.20-7.80 (m, 14H, ArH)	3365, 1614, 1547, 1594, 1463
8b	8.87 (s, 1H, NH), 8.41 (s, 1H, pyrazole-H), 7.10-7.90 (m, 13H, ArH), 2.31 (s, 3H, CH_3)	3358, 1602, 1540, 1604, 1448
8c	8.94 (s, 1H, NH), 8.55 (s, 1H, pyrazole-H), 7.00-7.90 (m, 13H, ArH), 2.30 (s, 3H, CH_3)	3347, 1631, 1533, 1592, 1453
8d	9.18 (s, 1H, NH), 8.52 (s, 1H, pyrazole-H), 7.00-7.90 (m, 13H, ArH)	3451, 1627, 1548, 1606, 1457

4 h and allowed to cool to room temperature. The separated solid product was filtered, washed with ethanol, dried and crystallized from dichoromethane-ethanol.

3. Synthesis of 2-Arylamino-5-(3-aryl-1-phenyl-pyrazol-4-yl)-1,3,4-thiadiazoles (6a-6d, 7a-7d, 8a-8d)

To a well stirred solution of the thiosemicarbazone (**3-5**) (1 mmol) in ethanol (10 mL) was added aqueous solution of 0.5 M $FeCl_3$ (8 mL) dropwise. The reaction mixture was heated at 70-80 °C for 1.5 h and then cooled. The precipitating solid was collected by filtration and washed with water and ethanol. The collected solid was recrystallized from dimethylformamide-water to afford the corresponding pyrazolyl-substituted thiadiazole derivatives **6-8**.

The physical data of new compounds are listed in Table 1. The data of ^{1}H NMR and IR are listed in Table 2.

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