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Metal salt-catalyzed diazocoupling of 3-substituted-1*H*-pyrazol-2-in-5-ones in aqueous medium

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Abstract

Organic synthesis in water belongs to green chemistry. $AlCl_3$-catalyzed diazocoupling of 3-substituted-1*H*-pyrazol-2-in-5-ones (**1**) in water with different aryldiazonium salts yielded (5-hydroxy-3-substituted-1*H*-pyrazol-4-yl)-azobenzene derivatives (**2**) as colored products with high yields.

Keywords: $AlCl_3$-catalyst; Diazocoupling in water; 3-Substituted-1*H*-pyrazol-2-in-5-ones

1. Introduction

5-Pyrazolones are very important class of heterocycles due to their biological and pharmacological activities [1,2] which exhibit an anti-inflammatory [3], herbicidal [4], fungicidal [5], bactericidal [5], plant growth regulating properties [4] antipyretic [6] and protein kinase inhibitors [7]. Also, they are used as key starting material for the synthesis of commercial arylazopyrazolone dyes.

On the other hand, its well known that the most important commercial application of pyrazolinones is their use as good fastness dyestuffs for wool, cotton, silk, leather, rubber and synthetic polyamides (Nylons). Many azopyrazolone dyes have been utilized as chromogenic reagents for the colorimetric determinations [8,9] and as indicators for complexometric titrations [10]. Also, there are some arylazopyrazolone dyes having potent antimicrobial activities [11].

In recent years water has become an intriguing reaction medium, especially for metal salt catalyzed organic reactions [12,13]. In many cases the catalyst and/or the aqueous medium can be recovered and reused, thereby reducing the environment impact of this process [14–16].

Water as a reaction medium has particularly captured the interest of organic chemists [12,13,17,18] and reactions previously thought impossible in water are now a reality. Many Lewis acids work well in aqueous medium [19,20], and even $AlCl_3$, $SnCl_2$ and $TiCl_4$ which are previously used under anhydrous conditions are excellent catalysts in water [14].

One of the greatest advantages of aqueous media [21] with respect to organic solvents is the possibility to control and change the pH. These affect the acid/base equilibria and the nature and concentration of the active species, with dramatic effects on reaction rates and product selectivity [22]. Therefore, we reported here the synthesis of many new 4-arylazo-3-substituted-1*H*-2-pyrazolin-5-ones in water that might be used as useful azodyes.

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2. Experimental

All melting points reported are uncorrected. IR spectra were recorded using Perkin Elmer's Spectrum RXIFT-IR spectrophotometer (ν in cm^{-1}) The NMR spectra were recorded on Bruker Avance DPX400 spectrometer, using pyridine-d_5 as a solvent and TMS as an internal standard (chemical shifts in δ values in ppm). Elemental analyses were preformed on Perkin Elmer 2400, series II micro-analyzer.

*2.1. Condensation of β-ketoester with hydrazine hydrate: formation of 5-hydroxy-3-substituted-1H-pyrazoles (**1a–c**)*

A solution of ethyl acetoacetate, (0.01 mol, 1.54 g), ethyl benzoylacetate (0.01 mol, 1.92 ml) or ethyl nicotinoylacetate (0.01 mol, 1.94 g) and hydrazine hydrate (0.01 mol, 0.48 g, 100%) in ethanol (50 ml) was refluxed for 6 h then the solvent was evaporated. The solid residue was crystallized from ethanol to give the corresponding pyrazole (**1a–c**) as white crystals.

*2.1.1. 5-Hydroxy-3-methyl-1H-pyrazoles (**1a**)*

White crystals from ethanol; $C_4H_6N_2O$ (98.10), Calcd.: C, 48.97, H, 6.16, N, 28.55; found: C, 48.72, H, 6.03, N, 28.41; yield 60%; m.p. 218–220 °C; IR (KBr), 3320–3340 (ν OH or NH), 1650 (ν C=O of pyrazolinone ring), 1590–1605 (ν C=C or C=N); ^{1}H NMR, δ (DMSO, ppm), 2.09 (s, 3H, CH_3), 3.35 (s, 1H, O*H*), 5.21 (s, 1H, C_4–*H*) and 10.32 (broad, 1H, N*H*); ^{13}C NMR, δ (DMSO, ppm), 11.84 (CH_3), 99.53 (C_4), 139.9 (C_3) and 161.6 (C_5).

*2.1.2. 5-Hydroxy-3-phenyl-1H-pyrazoles (**1b**)*

White crystals from ethanol; $C_9H_8N_2O$ (160.18), Calcd.: C, 67.49, H, 5.03, N, 17.49; found: C, 67.31, H, 4.96, N, 17.33; yield 65%; m.p. 238–240 °C; IR (KBr), 3320–3340 (ν OH or NH), 1650 (ν C=O of pyrazolinone ring), 1590–1605 (ν C=C or C=N); ^{1}H NMR, δ (DMSO, ppm), 5.96 (s, 1H, C_4–*H*), 7.34 (s, 1H, O*H*), 7.40–7.73 (m, 5H, Ar–*H*) and 11.2 (broad, 1H, N*H*); ^{13}C NMR, δ (DMSO, ppm), 87.59 (C_4), 125.4, 128.5, 129.5, 131.1 (phenyl carbons), 144.04 (C_3) and 161.74 (C_5).

*2.1.3. 5-Hydroxy-3-pyrid-3-yl-1H-pyrazoles (**1c**)*

White crystals from ethanol; $C_8H_7N_3O$ (161.16), Calcd.: C, 59.62, H, 4.38, N, 26.07; found: C, 59.44, H, 4.32, N, 25.92; yield 55%; m.p. 260–261 °C; IR (KBr), 3320–3340 (ν OH or NH), 1650 (ν C=O of pyrazolinone ring), 1590–1605 (ν C=C or C=N); ^{1}H NMR, δ (DMSO, ppm), 3.45 (s, 1H, O*H*), 6.03 (s, 1H, C_4–*H*), 7.44 (m, 1H, pyrid–C_5–*H*), 8.08 (d, 1H, pyrid–C_4–*H*), 8.51 (d, 1H, pyrid–C_6–*H*), 8.99 (s, 1H, pyrid–C_2–*H*) and 10.96 (s, 1H, N*H*); ^{13}C NMR, δ (DMSO, ppm), 87.59 (C_4), 125.4, 128.5, 129.5, 131.1 (phenyl carbons), 144.04 (C_3) and 161.74 (C_5).

*2.2. Diazocoupling of 3-substituted-2-pyrazolin-5-one (**1a–c**): formation of (5-hydroxy-3-substituted-1H-pyrazol-4-yl)-azobenzene derivatives (**2a–u**)*

4-Arylazo derivatives (**2a–u**) of 3-substituted-2-pyrazolin-5-one (**1a–c**) were prepared by coupling of the respective pyrazolinone with a freshly prepared solution of the desired diazonium salt in an ice path. Namely, 4-methyl, 4-bromo, 4-hydroxy, 4-acetyl, 2-carboxy, 2-carbomethoxy benzenediazonium chlorides and α-naphthyl diazonium chloride in water and in the presence of $AlCl_3$.

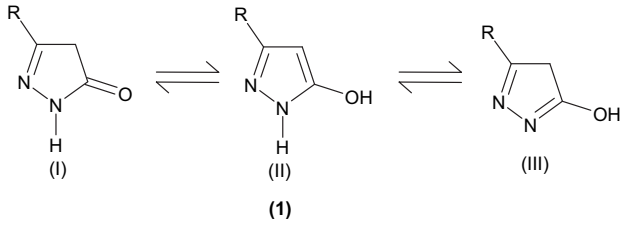
The desired aromatic amine (0.015 mol) was dissolved in concentrated hydrochloric acid (2 ml), diluted by water (20 ml) and cooled at 5 °C in an ice-bath. An aqueous cold solution of sodium nitrite (0.015 mol in 20 ml water) was added to the prepared aromatic amine hydrochloride to give the desired diazonium chloride solution. The latter solution was added drop-wise with stirring for 30 min in an ice-bath to a cold solution of 5-hydroxy-3-substituted-1*H*-pyrazoles (**1a–c**, 0.01 mol) in water (50 ml) containing $AlCl_3$ (3.0 g). The pH of the reaction mixture was kept at pH 3–4. After complete addition, the precipitated dyes were filtered, washed with water (3 × 25 ml) and dried. The solid products (**2a–u**) are crystallized from ethanol. The results are listed in Table 2.

3. Result and discussion

After long investigations using different metal salts at different pH values, we found that under acidic conditions pH ≤ 4.0, a heterogeneous reaction in aqueous medium of aromatic diazonium chlorides are coupled with 3-substituted-1*H*-pyrazol-2-in-5-ones (**1a–c**) at 0–5 °C in the presence of aluminum chloride ($AlCl_3$) as catalyst to give the colored 4-(5-hydroxy-3-substituted-1*H*-pyrazol-4-yl)-azobenzene (**2a–u**). No coloration or formation of azopyrazolones in aqueous medium in the absence of $AlCl_3$ was observed.

In continuation to our interest in pyrazolone chemistry [23–25], we have reported here the synthesis of some new intensively colored 4-(5-hydroxy-3-substituted-1*H*-pyrazol-4-yl)-azobenzene (**2**) in water that might be used as commercial dyes.

The 3-substituted-1*H*-pyrazol-2-in-5-ones (**1a–c**) existed in three tautomeric forms (**I–III**) due to their keto–enol or lactam–lactim tautomerism, while the full aromatic enol form (**II**) is the predominate one (Scheme 1). This phenomenon is confirmed by IR absorption spectra which showed absorption bands at ν (cm^{-1}):



Scheme 1.

1224–1248 (C=N exocyclic), 1360–1496 (N=N sym), 1547–1551 (N=N asym), 1596–1602 (C=C, C=N), 1661–1675 (C=O, cyclic amide of pyrazolone), 2610–3003 (CH), and 3235–3362 (NH or OH).

The approach reported here deals with the facile synthesis of some intensely colored 4-arylazo-3-substituted-5-hydroxy-1*H*-pyrazoles (**2a–u**) that might be used as commercial dyes in aqueous medium. A cold solution of aryldiazonium chlorides of primary aromatic amines; namely, *p*-toulidine, α-naphthylamine, *p*-bromoaniline, *p*-aminophenol, *p*-aminoacetophenone, anthranilic acid and methyl anthranilate which are prepared by treatment of sodium nitrite solution with the hydrochloride solution of primary amines, are coupled at C4 of a cold solution of 5-hydroxy-3-substituted-1*H*-pyrazole (**1a–c**) in water in the presence of $AlCl_3$ as catalyst to give a tautomeric mixture of 4-arylazo-3-substituted-1*H*-pyrazol-2-in-5-ones (**2a**), 4-arylazo-3-substituted-5-hydroxy-1*H*-pyrazoles (**2b**), and the more stable and predominant tautomer 4-(5-hydroxy-3-substituted-1*H*-pyrazol-4-yl)-azobenzene (**2c**) and **2d**.

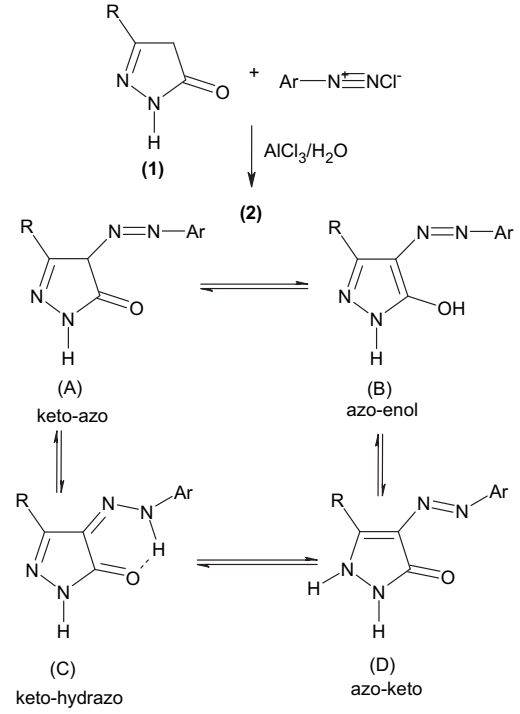
The dyes may exist in four possible tautomeric forms, namely two azo-keto forms **A** and **D**, the azo-enol form **B** and the hydazone-keto form **C**, as shown in Scheme 2. The deprotonation of the four tautomers leads to a common anion.

Numerous investigations were carried out to establish the tautomeric structures of arylazo-5-pyrazolones both in the solid state and in solution using a variety of spectroscopic techniques. The spectral data generally leads to the conclusion that the tautomeric equilibrium of the arylazopyrazolone dyes is in favor of the hydrazone form in the solid state and also in $CHCl_3$, DMSO and pyridine [26–28].

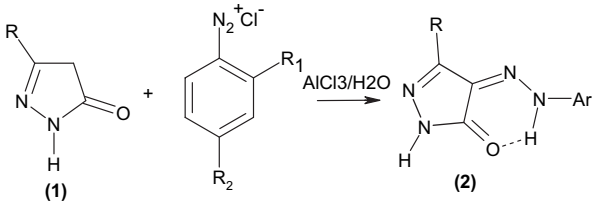
Our spectral data proved that the 4-arylhydrazopyrazolones (**C**) are the existed structure of the synthesized dyes due to their stabilization by intramolecular hydrogen bonding (Scheme 3).

The color of the synthesized arylazopyrazolones (**2a–u**) ranges from yellow to brown-red crystals.

The structures of arylhydrazopyrazolones (**2a–u**) have been confirmed by NMR (Table 1), IR spectral data and elemental analysis (Table 2).



Scheme 2.



a, R = methyl
b, R = phenyl
c, R = pyrid-3-yl

	R	Ar
a	CH_3	C_6H_4-CH_3,4-
b	CH_3	α-naphthyl
c	CH_3	C_6H_4-Br,4-
d	CH_3	C_6H_4-OH,4-
e	CH_3	C_6H_4-$COCH_3$,4-
f	CH_3	C_6H_4-COOH,2-
g	CH_3	C_6H_4-$COCH_3$,2-
h	C_6H_5	C_6H_4-CH_3,4-
i	C_6H_5	α-naphthyl
j	C_6H_5	C_6H_4-Br,4-
k	C_6H_5	C_6H_4-OH,4-
l	C_6H_5	C_6H_4-$COCH_3$,4-
m	C_6H_5	C_6H_4-COOH,2-
n	C_6H_5	C_6H_4-$COCH_3$,2-
o	Pyrid-3-yl	C_6H_4-CH_3,4-
p	Pyrid-3-yl	α-naphthyl
q	Pyrid-3-yl	C_6H_4-Br,4-
r	Pyrid-3-yl	C_6H_4-OH,4-
s	Pyrid-3-yl	C_6H_4-$COCH_3$,4-
t	Pyrid-3-yl	C_6H_4-COOH,2-
u	Pyrid-3-yl	C_6H_4-$COCH_3$,2-

Scheme 3.

Table 1
NMR-spectral data of compound **2**

Compd.	^{1}H NMR/δ (ppm)[a]
2a	2.20 (s, 3H, C_3-CH_3), 2.29 (s, 3H, Ph−CH_3), 7.16−7.40 (m, 4H, Ar−*H*), and 12.98 (s, 1H, N*H*)
2d	2.31 (s, 3H, C_3-CH_3), 7.19−7.47 (m, 4H, Ar−*H*), 11.92 (br, 1H, O*H*), and 12.91 (s, 1H, N*H*)
2e	2.27 (s, 3H, C_3-CH_3), 2.54 (s, 3H, $COCH_3$), 7.54 (d, 2H, Ar−*H*), 8.12 (d, 2H, Ar−*H*), and 13.16 (s, 1H, N*H*)
2g	2.29 (s, 3H, C_3-CH_3), 3.90 (s, 3H, $COOCH_3$), 7.15−7.56 (m, 4H, Ar−*H*), 13.06 (s, 1H, N*H*), and 14.84 (s, 1H, N*H* or O*H*)
2h	2.20 (s, 3H, Ph−CH_3), 7.17−7.56 (m, 9H, Ar−*H*), and 13.60 (s, 1H, N*H*)
2i	2.31 (s, 3H, $COCH_3$), 7.19−8.15 (m, 9H, Ar−*H*), 12.94 (s, 1H, N*H*), and 15.41 (br, 1H, N*H* or O*H*)
2m	7.19−8.44 (m, 9H, Ar−*H*), 13.54 (s, 1H, N*H*), and 14.95 (br, 1H, N*H* or O*H*)
2n	3.92 (s, 3H, $COOCH_3$), 7.18−8.44 (m, 9H, Ar−*H*), 13.82 (s, 1H, N*H*), and 15.32 (s, 1H, N*H* or O*H*)
2o	2.57 (s, 3H, Ph−CH_3), 7.15−7.78 (m, 4H, Ph−*H*), 8.95−10.13 (m, 4H, pyridyl−*H*), and 14.10 (s, 1H, N*H*)
2r	6.98 (s, 1H, O*H*), 7.15−7.50 (m, 4H, Ph−*H*), 8.61−9.79 (m, 4H, pyridyl−*H*), and 13.75 (br, 1H, N*H*)
2s	2.72 (s, 3H, CO−CH_3), 7.55−7.86 (m, 4H, Ph−*H*), 8.09−9.07 (m, 4H, pyridyl−*H*), and 13.76 (s, 1H, N*H*)

[a] The ^{1}H NMR of arylhydrazopyrazolones (**2**) have been measured in pyridine-d_5, therefore, water impurities in solvent appeared at δ 5.03−5.11 ppm and the protons of non-deuterated pyridine appeared at δ 7.15−7.20 (C_3-H), 7.52−7.62 (C_4-H) and 8.70−8.75 (C_2-H).

Table 2
Physical data of 4-arylhydrazo-3-substituted-1*H*-pyrazol-2-en-5-one derivatives (**2a−u**)

Product No.	M. Formula (m. wt.)	M.p. (°C) (color)	Yield %	Elemental analysis calc. (found)		
				C%	H%	N%
2a	$C_{11}H_{12}N_4O$ (216.24)	195−196 (Orange)	87	61.09 (60.93)	5.59 (5.47)	25.91 (25.77)
2b	$C_{14}H_{12}N_4O_2$ (268.26)	247−248 (Brown-red)	84	62.68 (62.53)	4.50 (4.41)	20.88 (20.72)
2c	$C_{10}H_9N_4OBr$ (281.11)	231−232) (Brown)	88	42.73 (42.57)	3.22 (3.20)	19.93 (19.69)
2d	$C_{10}H_{10}N_4O_2$ (218.21)	245−246 (Orange red)	82	55.04 (54.93)	4.62 (4.57)	25.67 (25.50)
2e	$C_{12}H_{12}N_4O_2$ (244.25)	233−235 (Yellow)	77	59.01 (58.87)	4.95 (4.82)	22.94 (22.77)
2f	$C_{10}H_{10}N_4O_3$ (246.22)	220−222 (Red)	84	53.60 (53.50)	4.09 (4.00)	22.75 (22.60)
2g	$C_{12}H_{12}N_4O_3$ (260.24)	224−225 (Yellow)	87	55.38 (55.26)	4.65 (4.58)	21.52 (21.37)
2h	$C_{16}H_{14}N_4O$ (278.30)	210−211 (Orange)	83	69.05 (68.88)	5.07 (5.02)	20.13 (20.00)
2i	$C_{19}H_{14}N_4O_2$ (330.33)	225−226 (Brown-red)	81	69.08 (68.93)	4.27 (4.19)	16.95 (16.75)
2j	$C_{15}H_{11}N_4OBr$ (343.18)	240−241 (Orange red)	87	52.49 (52.34)	3.23 (3.20)	16.32 (16.19)
2k	$C_{15}H_{12}N_4O_2$ (280.28)	238−239 (Orange red)	89	64.27 (64.11)	4.31 (4.27)	19.98 (19.78)
2l	$C_{17}H_{14}N_4O_2$ (306.32)	258−260 (Orange red)	82	66.65 (66.50)	4.60 (4.54)	18.29 (18.07)
2m	$C_{16}H_{12}N_4O_3$ (308.29)	265−266 (Brown-red)	81	62.33 (62.17)	3.92 (3.87)	18.17 (18.00)
2n	$C_{17}H_{14}N_4O_3$ (322.30)	263−264 (Yellow)	85	63.35 (63.30)	4.37 (4.30)	17.38 (17.29)
2o	$C_{16}H_{13}N_5O$ (279.29)	210−211 (Orange)	83	64.50 (64.38)	4.69 (4.61)	25.07 (24.93)
2p	$C_{18}H_{14}N_4O_2$ (331.32)	225−226 (Brown-red)	80	65.25 (65.48)	3.95 (3.99)	21.13 (22.21)
2q	$C_{15}H_{10}N_5OBr$ (345.17)	240−241 (Brown)	85	48.71 (48.73)	3.21 (3.19)	20.28 (20.22)
2r	$C_{14}H_{11}N_5O_2$ (293.28)	236−237 (Brown-red)	85	61.43 (61.27)	3.78 (3.72)	23.88 (23.17)
2s	$C_{16}H_{13}N_5O_2$ (307.30)	275−276 (Orange)	80	62.53 (62.44)	4.26 (4.18)	22.78 (22.60)
2t	$C_{15}H_{11}N_5O_3$ (309.28)	285−286 (Orange)	77	58.25 (58.10)	3.58 (3.51)	22.64 (22.53)
2u	$C_{16}H_{13}N_5O_3$ (323.31)	263−264 (Orange)	89	59.44 (59.36)	4.05 (4.00)	21.66 (21.50)

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