Effect of Metal Ions in Organic Synthesis; XX[1]. A Mild, Simple and Convenient Synthesis of Some 2-Arylaminohydrazones by Copper(II) Chloride-Catalyzed 1,4-Addition of Aromatic Amines to Arylazoalkenes

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In our previous papers, some reactions of arylazoalkene derivatives in the presence of metal ions have been reported. In particular, the stereospecific 1,4-conjugate additions (Michael type) of alcohols, water, and phenol to the azo-ene system of phenylazostilbene were examined[2]. More recently, the reaction of some arylazoalkenes with β-dicarbonyl compounds[3] and 3-oxoalkanamides[4] in the presence of copper(II) chloride dihydrate was presented. From these reactions useful intermediates and products have been obtained.

In continuation of these investigations, the 1,4-conjugate addition of some aromatic amines (**2**) to the azo-ene system of arylazoalkenes (**1**) in the presence of catalytic amounts of copper(II) chloride dihydrate (ratio **1**/catalyst from 1/0.2 to 1/0.04) has been studied. While no reaction occurs in the absence of the inorganic salt, the presence of copper(II) ions promotes the reaction, affording the 2-arylaminohydrazone derivatives (**3**) in moderate to good yields.

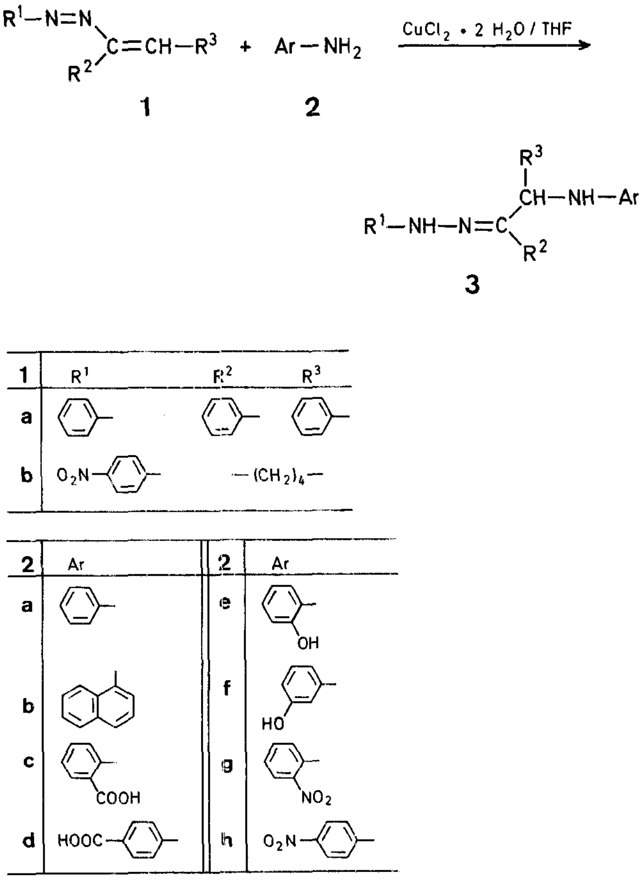

Table 1. 2-Arylaminohydrazones (**3**) prepared

Educts	Ratio of **1**: $CuCl_2 \cdot H_2O$	Reaction time	Product	Yield[a] [%]	m.p. [°C][b]	Molecular formula[c]
1a + **2a**	1:0.2	1 h	**3aa**	45	oil	$C_{26}H_{23}N_3$ (377.5)
1a + **2b**	1:0.2	2 h	**3ab**	30	oil	$C_{30}H_{25}N_3$ (427.6)
1a + **2c**	1:0.2	1 h	**3ac**	60	173–175°	$C_{27}H_{23}N_3O_2$ (421.5)
1a + **2d**	1:0.2	1 h	**3ad**	69	140–148°	$C_{27}H_{23}N_3O_2$ (421.5)
1a + **2e**	1:0.2	1 h	**3ae**	50	oil	$C_{26}H_{23}N_3O$ (393.5)
1a + **2f**	1:0.2	1 h	**3af**	45	oil	$C_{26}H_{23}N_3O$ (393.5)
1a + **2g**	1:0.2	2 h	**3ag**	55	137°	$C_{26}H_{22}N_4O_2$ (422.5)
1a + **2h**	1:0.2	1 h	**3ah**	65	219–222°	$C_{26}H_{22}N_4O_2$ (422.5)
1b + **2a**	1:0.04	2 h	**3ba**	62	oil	$C_{18}H_{20}N_4O_2$ (324.4)
1b + **2c**	1:0.04	1 h	**3be**	94	141–143°	$C_{19}H_{20}N_4O_4$ (368.4)
1b + **2d**	1:0.04	1 h	**3bd**	88	157–159°	$C_{19}H_{20}N_4O_4$ (368.4)
1b + **2e**	2:0.04	2 h	**3be**	75	oil	$C_{18}H_{20}N_4O_3$ (340.4)
1b + **2f**	1:0.04	2 h	**3bf**	80	184–186°	$C_{18}H_{20}N_4O_3$ (340.4)
1b + **2g**	1:0.04	2 h	**3bg**	51	213–215°	$C_{18}H_{19}N_5O_4$ (369.4)
1b + **2h**	1:0.04	2 h	**3bh**	69	203–205°	$C_{18}H_{19}N_5O_4$ (369.4)

[a] Yield of isolated pure products.

[b] M.p. are uncorrected.

[c] Satisfactory microanalysis obtained: C, ±0.35; H, ±0.30; N, ±0.30.

Table 2. Spectral Data of Compounds **3**

Product	I.R. ν [cm^{-1}]	^{1}H-N.M.R. (solvent/TMS$_{int}$) δ [ppm]
3aa	(film) 3330, 3410	($CDCl_3$) 5.35 (s, 1 H); 6.4–8.2 (m, 22 H)
3ab	(film) 3340, 3420	($CDCl_3$) 5.47 (s, 1 H); 6.1–8.4 (m, 24 H)
3ac	(Nujol) 3330, 3360	(DMSO-d_6) 5.65 (d, $J = 9.1$ Hz, 1 H), 6.1–8.0 (m, 19 H); 8.73 (s, 1 H)[a]; 9.55 (d, $J = 8.2$ Hz, 1 H)[a]
3ad	(Nujol) 3340, 3380	(DMSO-d_6) 5.6 (d, $J = 8.1$ Hz, 1 H); 6.55–8.0 (m, 20 H); 8.72 (s, 1 H)[a]
3ae	(film) 3310, 3410	($CDCl_3$) 4.95 (br. s, 1 H)[a]; 5.50 (d, $J = 21.6$ Hz, 1 H); 6.3–8.0 (m, 21 H)
3af	(film) 3320, 3420	($CDCl_3$) 4.9 (br. s, 1 H)[a]; 5.53 (d, $J = 31.8$ Hz, 1 H); 6.0–8.0 (m, 21 H)
3ag	(Nujol) 3345, 3430	(DMSO-d_6) 5.9 (d, $J = 8.1$ Hz, 1 H); 6.2–8.3 (m, 20 H); 9.0 (s, 1 H)[a]; 10.0 (d, $J = 8.2$ Hz, 1 H)[a]
3ah	(Nujol) 3320, 3380	(DMSO-d_6) 5.7 (d, $J = 9.1$ Hz, 1 H); 6.0–8.3 (m, 21 H); 8.75 (s, 1 H)[a]
3ba	(film) 3350, 3460	($CDCl_3$) 1.1–3.1 (m, 8 H); 4.0 (br. s, 1 H); 6.2–8.45 (m, 11 H)
3bc	(Nujol) 3340, 3380	(DMSO-d_6) 0.7–3.6 (m, 8 H), 4.25 (br. s, 1 H); 6.4–8.3 (m, 8 H); 8.9 (s, 1 H)[a]; 10.3 (s, 1 H)[a]
3bd	(Nujol) 3350, 3385	(DMSO-d_6) 0.9–3.6 (m, 8 H); 4.2 (br. s, 1 H); 6.5–8.3 (m, 9 H); 10.2 (s, 1 H)[a]
3be	(film) 3365, 3460	($CDCl_3$) 0.6–3.5 (m, 8 H); 3.8 (br. s, 1 H); 6.5–8.5 (m, 11 H)
3bf	(Nujol) 3340, 3430	(DMSO-d_6) 0.7–3.7 (m, 8 H); 4.05 (br. s, 1 H); 5.63 (br. s, 1 H)[a]; 5.8–8.4 (m, 8 H); 8.93 (s, 1 H)[a]; 10.15 (s, 1 H)[a]
3bg	(Nujol) 3350	(DMSO-d_6) 0.6–3.1 (m, 8 H); 4.5 (br. s. 1 H), 6.5–8.4 (m, 8 H); 9.2 (d, $J = 9.2$ Hz, 1 H)[a]; 10.33 (s. 1 H)[a]
3bh	(Nujol) 3310, 3380	(DMSO-d_6) 0.6–3.1 (m, 8 H); 4.6 (br. s, 1 H); 6.6–8.8 (m, 8 H); 10.8 (br. s, 2 H)[a]

[a] Exchangeable with D_2O.

These reactions take place under very mild conditions (magnetic stirring at room temperature) in the absence of a strong acid or base. No expensive or difficultly available reagents are necessary and the work-up procedure is easily performed. The amounts of copper(II) chloride dihydrate are always much less than stoichiometric, supporting the hypothesis of a catalytic role for the copper(II) ions. Probably, the ease with which these reactions proceed may be ascribed to a higher reactivity between arylazoalkenes (**1**) and amines (**2**) when the educts are present in the form of their organometallic complexes. In fact, it has been demonstrated that these compounds form complexes with several metal ions, in particular with copper(II) ions. In accordance with our previous findings in analogous reactions[2–5], it is assumed that the metal ion is regenerated in an active form during the reaction and catalyzes the conversion until completion.

It is worth noting, that aromatic amines containing electron-withdrawing groups in the benzene ring can be used in the catalytic 1,4-additions.

The 1,4-additions of nucleophiles to the azo-ene-system confirm that azoalkene derivatives are useful intermediates in organic synthesis affording *C*-functionalized hydrazone derivatives. As previously discussed[2–6], these compounds can be applied to intramolecular reactions yielding interesting heterocycles. Thus, 2-arylaminohydrazone derivatives may be utilized for the preparation of imidazolidones[7]. Furthermore, some of the 2-arylaminohydrazones (**3**) prepared by our method are of interest for the synthesis of 2-arylamino ketones which are difficult to obtain by other methods[8]. In fact, several recent methods are described in the literature[9] for the generation of the parent carbonyl compounds from their hydrazone derivatives.

The azoalkenes (**1**) are prepared as previously[2,3,4,10] reported. Commercially available amines (**2**) are used without further purification.

2-Arylaminohydrazone Derivatives 3; General Procedure:
Copper(II) chloride dihydrate (0.21 or 0.042 mmol; see Table 1) dissolved in tetrahydrofuran (15 ml) is added to a solution of the amine (**2**; 1.2 mmol) in tetrahydrofuran (15 ml). After magnetic stirring at room temperature for 5 min, a solution of the arylazoalkene (**1**; 1.05 mmol) in tetrahydrofuran (15 ml) is added. Stirring is continued at room temperature for 1–2 h (see Table 1) until the reaction is complete (monitored by silica gel T.L.C). The mixture is concentrated to a small volume under reduced pressure with gentle heating. The residue is shaken with benzene (100 ml) and water (100 ml). The benzene layer is separated, washed with water (2 × 100 ml) containing 1 normal hydrochloric acid (1 ml), and then with water

(2 × 50 ml). The organic extract is dried with sodium sulfate and evaporated under reduced pressure with mild heating. In general, the crude reaction products **3** are purified by distillation or recrystallization from methanol or benzene. In some cases, preliminary purification by column chromatography on silica gel may be necessary (elution with benzene or cyclohexane/benzene mixtures).

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