One-Pot Synthesis of 2-Aryl-3-phenyl(benzyl)-5-phenylimino-Δ^4-1,2,4-thiadiazolines using *N*-Chlorosuccinimide

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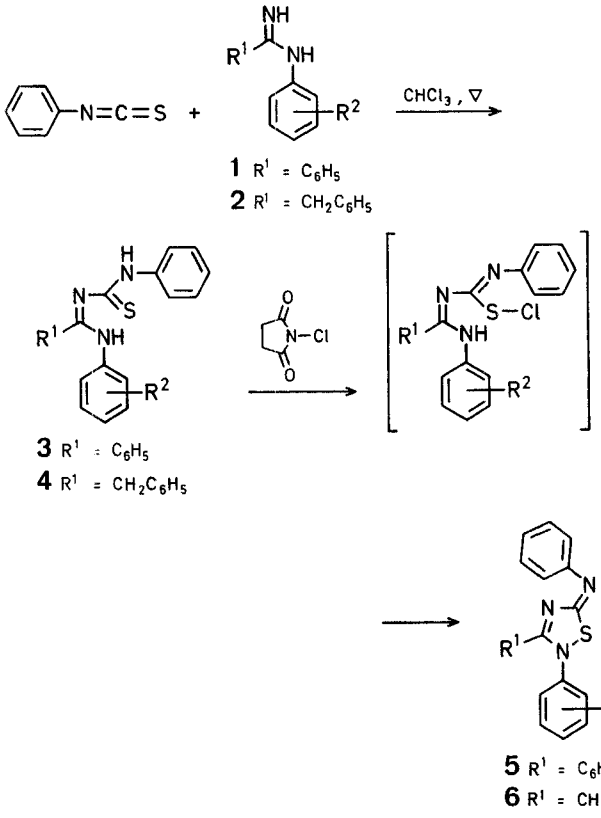
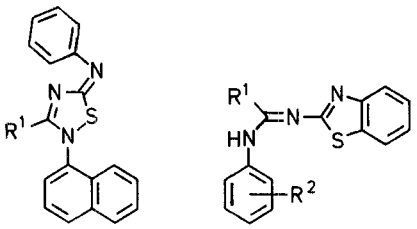
A number of methods have been reported concerning the synthesis of 3,5-disubstituted 1,2,4-thiadiazoles and almost all of them have been utilised with varying degrees of success[1-4]. Oxidative cyclisation of the readily accessible amidinothioureas has been known to be the general route for the synthesis of 3,5-disubstituted 1,2,4-thiadiazoles and best yields have been reported with bromine. The overall yields varied between 40–64% considering the amount of amidine used in the reaction[5]. It has also been reported that the monosubstituted amino group (e.g. anilino) in the amidinothiourea can also participate in cyclisation[6], as shown by the ready oxidation of 1-(*N,N'*-diphenylamidino)-3-phenylthiourea, but, in this case, the product obtained was 2-guanidinobenzothiazole. It was thus thought worthwhile to perform the oxidation of *N*-arylbenzimidoyl-*N'*-phenylthioureas **3** and *N*-arylphenylacetimidoyl-*N'*-phenylthioureas **4** in order to investigate the products formed in these cases.

Thus, we report here an efficient one-pot synthesis of the previously unknown 2-aryl-3-phenyl-5-phenylimino-Δ^4-1,2,4-thiadiazolines **5** and 2-aryl-3-benzyl-5-phenylimino-Δ^4-1,2,4-thiadiazolines **6** by the oxidation of substituted thioureas **3** and **4**, respectively, with *N*-chlorosuccinimide, in almost quantitative yields. The substituted thioureas **3** and **4** which are stable and isolable, have been prepared *in situ* by the reaction of phenyl isothiocyanate with the corresponding amidines **1** and **2**. The method has also been extended to the synthesis of 2-naphthyl-3-phenyl-5-phenylimino-Δ^4-1,2,4-thiadiazoline (**7**) and 2-naphthyl-3-benzyl-5-phenylimino-Δ^4-1,2,4-thiadiazoline (**8**).





The differentiation between (*E*)- or (*Z*)-forms of thiadiazolines **5**–**8**, on the basis of traditional techniques like low temperature ^{1}H-N.M.R. will perhaps be difficult, since only minor changes are expected in the chemical shifts of only the phenyl protons. However, on the basis of stereochemical studies for *N*-arylimines[7,8], where the phenyl group was shown to be *anti*- to the larger functional groups attached to the carbon atom of the imine, the phenyl group in thiadiazolines **5**–**8** is probably *anti*- to bigger sulfur atom. The identities of the 1,2,4-thiadiazolines **5**–**8** have been established on the basis of microanalyses and spectral data (Table).

It may be worthwhile to mention here that, on using bromine and *N*-bromosuccinimide as oxidising agents, the T.L.C. of the reaction mixture showed two spots of almost equal intensities, one corresponding to the 1,2,4-thiadiazoline and the other may be due to the 2-guanidinobenzothiazole (**9**).

The *N*-arylbenzamidines, *N*-arylphenylacetamidines were prepared by the reported method[9].

Table. Compounds **5–8** prepared

Product No.[a]	R^1	R^2	Yield [%]	m.p. [°C][b]	Molecular Formula[c]	^{1}H-N.M.R. ($CDCl_3$/TMS)[d] δ [ppm]
5a	C_6H_5	H	90	183–184°	$C_{20}H_{15}N_3S$ (329.4)	7.2 (m, H_{arom})
5b	C_6H_5	2-CH_3	98	178–180°	$C_{21}H_{17}N_3S$ (343.5)	1.96 (s, 3H, CH_3); 7.21 (m, 14H_{arom})
5c	C_6H_5	4-CH_3	91	187–189°	$C_{21}H_{17}N_3S$ (343.5)	1.85 (s, 3H, CH_3); 7.25 (m, 14H_{arom})
5d	C_6H_5	2-Cl	95	180–182°	$C_{20}H_{14}ClN_3S$ (363.9)	7.3 (m, H_{arom})
5e	C_6H_5	4-Cl	96	184–186°	$C_{20}H_{14}ClN_3S$ (363.9)	7.2 (m, H_{arom})
5f	C_6H_5	4-Br	95	184–185°	$C_{20}H_{14}BrN_3S$ (408.3)	7.1 (m, H_{arom})
5g	C_6H_5	2-OCH_3	95	188–189°	$C_{21}H_{17}N_3OS$ (359.5)	3.55 (s, 3H, OCH_3); 7.1 (m, 14H_{arom})
6b	$CH_2C_6H_5$	2-CH_3	95	160–161°	$C_{21}H_{19}N_3S$ (357.5)	1.95 (s, 3H, CH_3); 3.6 (s, 2H, CH_2); 7.2 (m, 14H_{arom})
6c	CH_2—C_6H_5	4-CH_3	95	153–155°	$C_{21}H_{19}N_3S$ (357.5)	1.88 (s, 3H, CH_3); 3.6 (s, 2H, CH_2) 7.15 (m, 14H_{arom})
6d	CH_2—C_6H_5	2-Cl	92	153–155°	$C_{21}H_{16}ClN_3S$ (376.9)	3.5 (s, 2H, CH_2); 7.2 (m, 14H_{arom})
6e	CH_2—C_6H_5	4-Cl	98	154–156°	$C_{21}H_{16}ClN_3S$ (376.9)	3.7 (s, 2H, CH_2); 7.2 (m, 14H_{arom})
6f	CH_2—C_6H_5	4-Br	96	152–154°	$C_{21}H_{16}BrN_3S$ (422.3)	3.5 (s, 2H, CH_2); 7.2 (m, 14H_{arom})
7	–	–	95	190–192°	$C_{24}H_{17}N_3S$ (379.5)	7.3 (m, H_{arom})
8	–	–	94	159–161°	$C_{25}H_{19}N_3S$ (393.5)	3.6 (s, 2H, CH_2); 7.2 (m, 17H_{arom})

[a] All the compounds reported in the Table have the following common I.R. and U.V. data which are comparable with the reported values[6] I.R. (KBr): ν = 3060 (C—H), 1595, 1550 and 1485 cm^{-1} (C=N, C=C); recorded on a Perkin-Elmer Model 297 infrared spectrophotometer. U.V. (CH_3OH): λ_{max} = 234 nm (log ε = 4.74); 274 nm (log ε = 4.68); recorded on a Beckmann-26 spectrophotometer.

[b] Uncorrected.

[c] Satisfactory microanalyses obtained: C ±0.16, H ±0.02, N ±0.03.

[d] Recorded on a Varian EM-390 90 MHz spectrometer.

2-Aryl-3-phenyl(benzyl)-5-phenylimino-Δ^4-1,2,4-thiadiazolines 5–8; General Procedure:

A solution of *N*-arylamidine **1** (0.02 mol) and phenyl isothiocyanate (2.7 g, 0.02 mol) in dry chloroform (20 ml) is refluxed till T.L.C. showed the disappearence of starting materials (~ 6 h). The mixture is then cooled to room temperature, *N*-chlorosuccinimide (2.19 g, 0.02 mol) is added, and the mixture is stirred at room temperature for 1 h. The mixture is washed with saturated solution of sodium hydrogen carbonate (2 × 25 ml) and water (2 × 50 ml). The chloroform layer is dried with anhydrous sodium sulphate. The solid so obtained after removal of chloroform is then recrystallised from benzene/hexane (1:1).

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