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NOTE

Synthesis of Some 2-Amino-5-Aryl-1,3,4-Thiadiazoles

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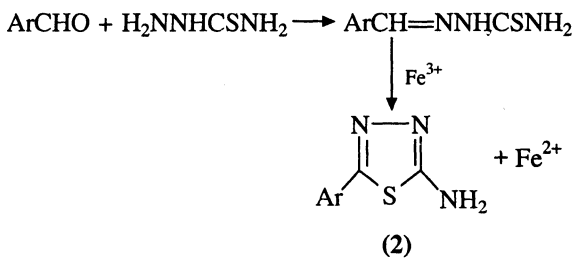
A few 2-amino-5-aryl-1,3,4-thiadiazoles have been synthesised by oxidative cyclization of aldehyde thiosemicarbazones with ferric chloride, making some modifications in the reported procedures.

Interesting pharmacological properties exhibited by 2-amino-5-aryl-1,3,4-thiadiazoles prompted a number of scientists to develop different viable and economical methods for its synthesis. These include (a) dehydrative cyclization of aroyl thiosemicarbazides[1–2] and (b) oxidative cyclization of thiosemicarbazones[3–6].

Literature survey reveals that the process of oxidative cyclization using ferric chloride poses a real challenge to the scientist to isolate quantitatively synthesised 1,3,4-thiadiazoles economically in minimum time. Each procedure has its own limitations. These include (i) removal of huge amount of water[3–5] or alcohol[6], (ii) frequent handling of concentrated hydrochloric acid[6], and (iii) removal of trace amount of iron residue from the final products[3–6].

Comparative study of the methods cited in literature using oxidative cyclization of aldehyde thiosemicarbanzones showed that the procedure of Ranga Rao and Srinivasan[6] gave the best yield. So this procedure was selected for comparative study. We report here the modifications made in the procedures to get better final products which involve separation of excess ferric ions (Fe^{3+}) and liberated ferrous ions (Fe^{2+}) with citric acid and sodium citrate[7].

The synthesis involve the oxidative cyclization of aldehyde thiosemicarbazones using ferric chloride as oxidising agent (Scheme-1).

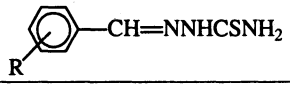


(Scheme-1)

The structures of the final compounds were established on the basis of elemental analysis and IR spectral data in KBr phase (Shimadzu IR 470 spectrophotometer). The melting points were determined by using open capillaries and are compared with reported ones.

Synthesis of thiosemicarbazones (1): Aromatic aldehyde (0.2 M) in warm alcohol (300 mL) and a solution of thiosemicarbazide (0.2 M) in 300 mL hot water were mixed slowly with continuous stirring. The product which separated was filtered off after cooling. The melting points are reported in Table-1.

TABLE-1
PHYSICAL PROPERTIES OF THIOSEMICARBAZONES



	R	Yield (%)	(Recryst.) solvent	m.p. (°C)	(%) Nitrogen (found/calcd.)
1.	H—	92	Aq. ethanol (50%)	159–160 (158.5–160)[4]	23.66 (23.46)
2.	*p*-CH_3—	95	Aq. ethanol (50%)	162 (160–161)[4]	21.58 (21.74)
3.	*p*-OCH_3—	94	Aq. ethanol (50%)	168–170	20.35 (20.09)
4.	*p*-Cl—	90	Ethanol	207–209 (209–210.5)[4]	19.48 (19.67)

m.p. in brackets are reported in ref. 4.

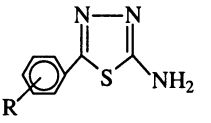
Synthesis of 2-amino-5-aryl-1,3,4-thiadiazoles (2): Thiosemicarbazone **1**, (0.05 M) was suspended in 300 mL distilled water in a one-litre beaker. Ferric chloride (0.15 M) in 300 mL distilled water was added to it. This was heated to 80–90°C and maintained for 45 minutes. Then using a hot water funnel, the solution was filtered. A mixture of citric acid (0.11 M) and sodium citrate (0.05 M) was added to the solution and stirred. After cooling the whole solution was divided into 4 parts, then neutralization was affected by aqueous ammonia (10%). The precipitate so obtained was filtered and washed with distilled water and allowed to dry. The final crystallization was affected by solvents given in Table-2.

All the compounds showed IR absorption bands at 3300 and 3100 cm^{-1} (due to N—H str of amino group), 1620–1600 cm^{-1} (N—H def.), 1300–1280 cm^{-1} (C—N str.), 1570 (C=C str., aromatic), 830–815 cm^{-1} (1,4-substituted phenyl gr.) and 760 cm^{-1} (monosubstituted phenyl group).

By this modifed procedure we have been successful in isolating 2-amino-5-aryl-1,3,4-thiadiazoles in good yield and in pure form. There has been no batch to batch variation, so common with earlier reported procedures. This method used only water (avoiding evaporation of it as suggested by earlier workers) as the medium and there is no extraction with any organic solvent, this makes it economical. There was no change in colour of the product, *i.e.*, batch to batch.

Last but not the least it is worth mentioning that the overall time required has also been reduced.

TABLE-2
PHYSICAL PROPERTIES OF 2-AMINO-5-ARYL-1,3,4-THIADIAZOLES



	R	Yield (%)	(Recryst.) solvent	m.p. (°C)	(%) Nitrogen (found/calcd.)
1.	H—	65 (50)	Aq. ethanol (25%)	224–225 (224)	23.88 (23.72)
2.	*p*-CH_3—	62 (55)	Aq. ethanol (25%)	214–215 (215–216)	22.15 (21.98)
3.	*p*-OCH_3—	60 (35)	Aq. ethanol (25%)	187–188 (185–187)	20.50 (20.28)
4.	*p*-Cl—	70 (65)	Aq. ethanol 50%	227–229 (229–230)	19.93 (19.85)

Yields and m.p. in brackets are those reported in ref. 6.

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