A Newer Synthesis of Formamidines Used as Acaricide-Insecticides

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There are valuable pesticides among the formamidines; e.g. chlordimeform, *N*'-(4-chloro-2-methylphenyl)-*N*,*N*-dimethylformamidine, used as an acaricide insecticide. Different procedures are known for the synthesis of formamidines, including those starting from the corresponding anilines and formamides in the presence of condensing reagents[1,2]. New syntheses have been described by Pedersen which involve reaction of acylanilides with dialkylformamides in the presence a large excess of hexamethylphosphoric triamide[3] or phosphorus pentoxide[4].

Table. Formamidines **5** prepared

Product	Ar	R^2	R^3	R^1 in 1 and 4	Method (solvent)	Reagent	Reaction conditions (temperature/time)	Yield [%]	b.p. [°C]/torr found	b.p. [°C]/torr reported	n_D^{20} (or m.p. [°C]) found	n_D^{20} (or m.p. [°C]) reported	Purity [%][b]
5a	2-H_3C—4-Cl—C_6H_3	CH_3	CH_3	CH_3	A (toluene)	**3b**	100 °C/1 h	87	101–104°/0.1	100–102°/0.1[4]	1.5932[a]	1.5914[4]	99.8
					B (none)	**3b**	100 °C/0.5 h	85		163–165°/14[6]	1.5938[b]	(32°)[6]	97.3
					A (toluene)	**3a**	100 °C/1 h	70			1.5964		97.1
					A (ClC_6H_5)	**3c**	100 °C/1 h	80			1.5920		98.3
5b	C_6H_5	CH_3	CH_3	CH_3	A (toluene)	**3b**	90 °C/2 h	89	75–77°/0.1	75–76°/0.2[7]	1.5964	(223–225°)[c,7]	97.8
5c	C_6H_5	CH_3	CH_3	$ClCH_2$	A (xylene)	**3b**	110 °C/4 h	85			1.5948		96.5
5d[d]	2,4-di-Cl—C_6H_3	CH_2SCH_3	CH_3	CH_3	A (toluene)	**3b**	100 °C/1 h	83	169–171°/0.1	157–158°/0.7[8]	—		97.2
5e[e]	2-H_3C—C_6H_4	C_2H_5	H	CH_3	B (none)	**3b**	100 °C/0.5 h	79	100–105°/0.1	—	—		97.0

[a] n_D^{35}.

[b] Purity by G.L.C. (Packard 421; FID, column 80 cm × 2 mm with 10% SE-30 on Chromosorb W 80/100 mesh, temp.: 190°/200°/250 °C.

[c] m.p. of hydrochloride.

[d]

$C_{10}H_{12}Cl_2N_2S$	calc.	C 48.20	H 4.85	N 28.46	Cl 5.62	S 12.87
(263.2)	found	48.53	4.89	28.29	5.77	12.78

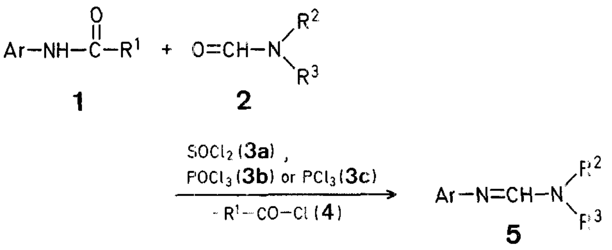
[e]

$C_{10}H_{14}N_2$	calc.	C 74.03	H 8.70	N 17.27
(162.2)	found	74.21	8.77	17.12

0039-7881/80/1132–0883 $ 03.00

Advantageous manufacturing methods for chlordimeform are the chlorination of N'-(2-methylphenyl)-N,N-dimethylformamidine or the condensation of 4-chloro-2-methylaniline with dimethylformamide. For the latter method, 4-chloro-2-methylaniline is produced by chlorination of 2-methylaniline with protection of the amino group by acylation.

In this communication it is shown that N'-aryl-N,N-dialkylformamidines **5** can be prepared directly from acylanilides **1** without removal of the protecting acyl group and with the simultaneous formation of acyl chlorides **4** in equimolar amounts.

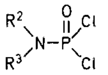


Formamidines **5** are now produced by heating acylanilides **1**, dialkylformamides **2**, and condensing reagents **3** in suitable solvents. The reaction can also be carried out in the absence of solvents.

The main advantages of this new synthesis are:

- the carboxylic acid used to protect the amino group can be recovered as acyl chloride,
- there is no need to use an excess of the condensing agent.

The mechanism of the reactions may be similar to one described by Pedersen[5]. Acylanilides and dialkylformamides are in equilibrium with formanilides and dialkylacylamides. Reagents **3** react with the latter compounds producing acyl chlorides **4** and the intermediate, such as **6** in the case of reagent **3b**. The intermediate reacts with the enol form of formanilides giving formamidines **5**.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Formamidines 5; General Procedures:

Method A: in a solvent: Reagent **3** (0.1 mol) is added dropwise to dialkylformamide **2** (0.1 mol) in the solvent (25 ml) at a temperature below 30 °C. This mixture is added to a suspension of the acylanilide **1** (0.1 mol) in the same solvent (50 ml) at the reaction temperature (Table). The mixture is heated at this temperature for the time given, the acyl chloride **4** is distilled, the reaction mixture is heated further, and then allowed to cool to 60 °C. Water (50 ml) is added dropwise to the mixture which is then stirred for 0.5 h. After separation, the aqueous phase is treated with 5 molar sodium hydroxide solution (100 ml) and is extracted with benzene (2 × 25 ml). The combined benzene phases are washed with water (25 ml), dried with sodium sulphate, and the benzene is evaporated. The residue is a pale brown oil of 97% purity as determined by G.L.C. (10% SE-30 on Chromosorb W 80/100 mesh, 190–250 °C); yield of **5**; 70–89%; yield of acyl chloride **4**: ~90%.

Method B: in the absence of solvent: Acylanilide **1** (0.1 mol) is dissolved in dialkylformamide **2** (0.1 mol) at 100 °C and phosphoryl chloride (**3b**; 9.2 ml, 0.1 mol) is added dropwise to the mixture during 0.5 h with simultaneous distillation of acyl chloride **4**. Further procedure is similar to that described above.

Received: December 20, 1979
(Revised form: June 19, 1980)

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