A Facile Synthesis of Acaricide-Insecticide and Defoliant *N'*,*N'*-Dimethylformamidines

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Formamidines of the chlordimeform type [*N*-(4-chloro-2-methylphenyl)-*N'*,*N'*-dimethylformamidine] are of increasing interest as acaricides, because the natural enemies of mites in the past have been controlled by insecticides[1,2]. In addition, trialkylformamidines have shown strong defoliant activity of cotton-wool[3]. Several procedures for the synthesis of formamidines starting from the corresponding anilines or formamides are known[3-7].

In electrophilic aromatic substitution reactions, such as chlorination, bromination, and nitration reactions, of anilines, the acetyl group is often used as a protecting group for the amino group. The protecting acetyl group is then removed by hydrolysis. In this communication it is shown that *N*-aryl-*N'*,*N'*-dimethylformamidines **3** can be prepared directly from acetanilides **1** without removal of the protecting acetyl group prior to the amidine synthesis.

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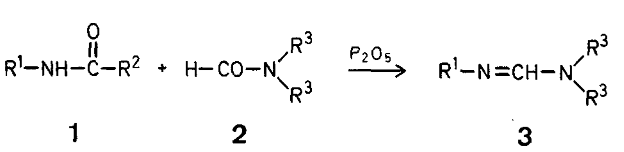
Table. Preparation of *N*′,*N*′-Dialkylformamidines **3**

Product	R^1	R^2 in **1**	R^3	Yield [%]	Reaction time	b.p./torr observed	b.p./torr Lit.	n_D^{25} or m.p. observed	n_D^{25} or m.p. Lit.
3a	C$_6$H$_5$	H	CH$_3$	27	2 h	70–72°/0.1	68–70°/0.08[7]	1.5932	1.5924[7]
3a	C$_6$H$_5$	CH$_3$	CH$_3$	89	2 h	—	—	—	—
3a	C$_6$H$_5$	C$_6$H$_5$	CH$_3$	41	216 h	—	—	—	—
3b	4-H$_3$C—C$_6$H$_4$	CH$_3$	CH$_3$	91	2 h	83–84°/0.1	77–79°/0.08[7]	1.5824	1.5828[7]
3b	4-H$_3$C—C$_6$H$_4$	C$_2$H$_5$	CH$_3$	91	2 h		—	—	—
3c	4-Br—C$_6$H$_4$	CH$_3$	CH$_3$	93	2 h	100–101°/0.06	105–110°/0.25[8]	1.6297	—
3d	4-C$_2$H$_5$O—C$_6$H$_4$	CH$_3$	CH$_3$	93	2 h	109–110°/0.1	—[a]	49–50°	—
3e	4-O$_2$N—C$_6$H$_5$	CH$_3$	CH$_3$	76	2 h	—	—	78–80°	77–78°[5]
3f	4-H$_3$CO—2-O$_2$N—C$_6$H$_3$	CH$_3$	CH$_3$	74	7 h	145–146°/0.05	141–160°/0.15[8]	1.6156	—
3g	4-Cl—2-H$_3$C—C$_6$H$_3$	CH$_3$	CH$_3$	83	2 h	100–102°/0.1	96–99°/0.08[7]	1.5914	1.5908[7]
3h	4-H$_3$C—3-Cl—C$_6$H$_3$	CH$_3$	CH$_3$	97	2 h	96–97°/0.05	102–104°/0.15–0.2[8]	1.5992	—
3i	*n*-C$_8$H$_{17}$	CH$_3$	CH$_3$	51	24 h	65–67°/0.1	75–78°/0.02[3]	1.4562	—
3j	*n*-C$_{12}$H$_{25}$	CH$_3$	CH$_3$	53	24 h	113–115°/0.1	—	1.4629[b]	1.4696[b,3]
3k	C$_6$H$_5$	CH$_3$	C$_2$H$_5$	79	2 h	145–147°/13	143–144°/15[9]	141–142°[c]	140–141°[c,9]

[a] $C_{11}H_{16}N_2O$ (192.3) calc. C 68.72 H 8.39 N 14.57; found C 68.82 H 8.48 N 14.55

[b] n_D^{20}.

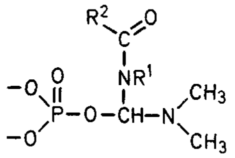
[c] m.p. of picrate.



$$R^1{-}NH{-}\overset{O}{\overset{\|}{C}}{-}R^2 + H{-}CO{-}N(R^3)_2 \xrightarrow{P_2O_5} R^1{-}N{=}CH{-}N(R^3)_2$$

Formamidines are now obtained by refluxing acetanilides **1** with phosphorus pentoxide in dimethylformamide (**2**, R^3 = CH$_3$). In all cases excellent yields of **3** were obtained. The formamidine synthesis appears to be quite general. It also proceeds for formyl-, propion-, and benzanilides. This procedure was extended to two trialkylformamidines of which *N*-dodecyl-*N*′,*N*′-dimethylformamidine has been reported as a strong defoliant[3]. The reaction of acetanilide also proceeds using diethylformamide and phosphorus pentoxide as reagents. Therefore, it may be inferred that the reaction is general for dialkylformamides.

In the reaction of benzanilide with dimethylformamide and phosphorus pentoxide, *N*,*N*-dimethylbenzamide was isolated as well as the expected formamidine. The mechanism may then be suggested as follows. A phosphorus pentoxide/dimethylformamide complex (Vilsmeier type, in analogy with phosphoryl chloride and dimethylformamide) attacks the nitrogen atoms of the carboxamide to give the intermediate **4**, in which the oxygen atoms can be attached to other phosphorus atoms or negatively charged. The amidine is then formed by splitting off a mixed anhydride between phosphoric acid and carboxylic acid. This anhydride then undergoes further reactions with dimethylformamide to produce *N*,*N*-dimethylcarboxamides.



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***N*′,*N*′-Dimethylformamidines 3:**

Carboxamide **1** (0.075 mol), phosphorus pentoxide (15 g), and dimethylformamide (**2**; 50 ml) [for preparation of **3k** diethylformamide (72 ml) is used] are heated under reflux with stirring. [For heating periods of more than 10 h an oil bath (200°) is used]. The mixture is allowed to cool to room temperature and is then poured into 1 molar sodium hydroxide (400 ml). The aqueous phase is extracted with ether (3 × 200 ml). The combined ether phases are washed with water (100 ml), dried with potassium carbonate, and distilled. (The crude **3e** is not distilled, but recrystallized from toluene/petroleum ether, b.p. 60–80°). Prior to the distillation the crude **3i** and **3j** are taken up in 4 normal hydrochloric acid (35 ml) and extracted with ether. The aqueous phase is then made alkaline with 2 molar sodium hydroxide and extracted with ether. The ether phase is dried with potassium carbonate and distilled. The same procedure is used, when benzanilide is used as starting material for preparation of **3a**. N,N-*Dimethylbenzamide* m.p. 39–40° (from ether/petroleum ether; Lit.[10] m.p. 41–43°), is then isolated from the ether phase used for extraction of the HCl-phase withholding the crude **3a**.

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