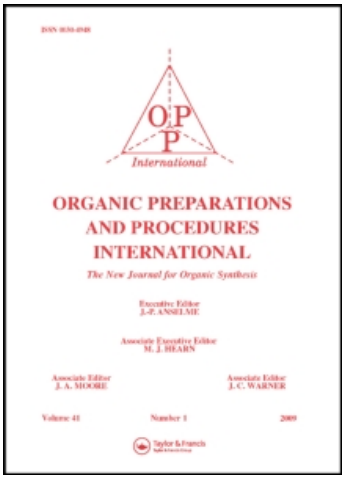

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PREPARATION OF N-UNSUBSTITUTED THIOAMIDES BY A MODIFIED WILLGERODT-KINDLER REACTION

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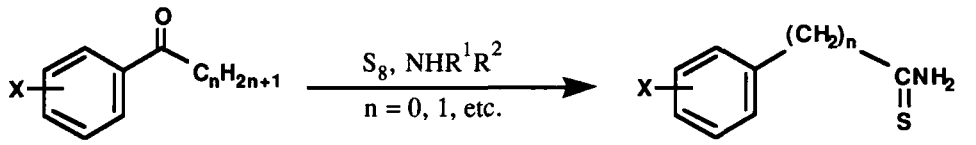
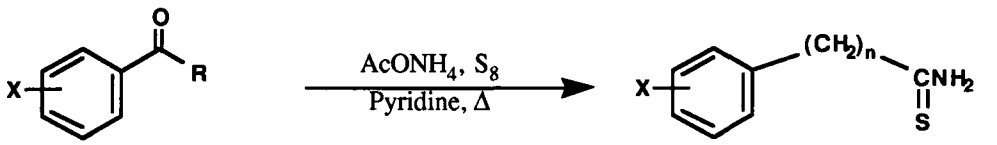
Thioamides are very useful intermediates[1] for organic synthesis and are prepared mainly a) by the reaction of amides with phosphorous pentasulfide[2] or Lawesson reagent[3], b) by the Willgerodt-Kindler reaction[4] and c) by the reaction of nitriles or cyanogen with hydrogen sulfide.[5] Among these, the Willgerodt-Kindler reaction is the better and more convenient procedure, for the preparation of thioamides from aromatic aldehydes or ketones by reaction with sulfur and amines. When high-boiling amines are used, the reaction may be carried out in normal equipment in high yields. However, in the case of ammonia and low-boiling amines, the reaction must be performed in autoclaves or sealed tubes, and these thioamides (especially the N-unsubstituted ones) were usually prepared by alternative methods. We now report a modified Willgerodt-Kindler reaction for the preparation of N-unsubstituted thioamides under normal pressure.



The thioamides maybe conveniently obtained by refluxing aromatic aldehydes or substituted acetophenones with sulfur, and ammonium acetate in pyridine. The results listed in Table 1 show that



1 **2**

R = H or CH_3, n = 0 or 1

the yields of thiobenzamides from aldehydes are higher than those of phenylthioacetamides from ketones. When **1k** or **1l** were used as substrates in this modified reaction, the expected thioamides **2k**

and **2l** could not be isolated. Instead of N-unsubstituted thioamides. N,N-dimethylthioamides were obtained when DMF was used as solvent in the reaction.[6] The expected N-unsubstituted thioamides were obtained when the solvent was changed from DMF to N,N-dimethylacetamide or pyridine. The yields were better in pyridine.

TABLE. Preparation of N-Unsubstituted Thioamides

	Material (1)	Product (2)	Yield (%)		Material (1)	Product (2)	Yield (%)
a	R = H X = H	n = 0 X = H	37	**g**	R = H X = 4-Br-	n = 0 X = 4-Br-	51
b	R = H X = 4-Cl	n = 0 X = 4-Cl-	33	**h**	R = CH_3 X = H	n = 1 X = H	19
c	R = H X = 4-CH_3O-	n = 0 X = 4-CH_3O-	32	**i**	R = CH_3 X = 4-Cl-	n = 1 X = 4-Cl-	37
d	R = H X = 4-CH_3-	n = 0 X = 4-CH_3	27	**j**	R = CH_3 X = 4-CH_3O-	n = 1 X = 4-CH_3O-	14
e	R = H X = 4-Me_2N-	n = 0 X = 4-Me_2N-	25	**k**	R = H X = 4-NO_2	n = 0 X = 4-NO_2	—
f	R = H X = 4-F_3C-	n = 0 X = 4-F_3C-	54	**l**	R = Et X = H	n = 2 X = H	—

EXPERIMENTAL SECTION

The melting points are uncorrected. ^1H NMR were determined on a Varian FT-80A and chemical shifts are reported in ppm downfield from TMS. MS were obtained on a Varian-M212.

General Procedure.- A mixture of an aromatic aldehyde or acetophenone (0.1 mol), sulfur (0.15 mol), ammonium acetate (0.15 mol) and pyridine 40 ml was heated slowly to refluxing (within 30-45 min) with stirring. The refluxing was continued until the aldehyde or ketone was consumed (TLC analysis). The reaction mixture was poured into water (300 ml) and the aqueous solution was extracted with toluene (30 ml x 4). The combined toluene layer was dried and distilled to remove organic solvents. The residue was treated with 95% ethanol and undissolved solid was removed with suction

filtration. From the filtrate, the product crystallized upon cooling.

Thiobenzamide, mp. 116-118° (from toluene), lit.[7a] mp. 116-117°. ^{1}H NMR ($CDCl_3$: DMSO-d_6 9:1): δ8.8 (s, 2H, NH_2), 8.0 (m, 2H, Ph-H), 7.5 (m, 3H), Ph-H). MS (m/z): 137 (M^+, 100%), 121, 104, 77.

4-Chlorothiobenzamide, mp. 132-133° (from ethanol), lit.[8] mp. 129-130°. ^{1}H NMR ($CDCl_3$: DMSO-d_6 1:1): δ 9.2-9.5 (s, 2H, NH_2), 8.0 (d, 2H, Ph-H), 7.4 (d, 2H, Ph-H). MS (m/z): 171 (M^+, 100%), 155, 138, 111, 75, 60.

4-Methoxythiobenzamide, mp. 152-153° (from water-dioxane 3:2), lit.[8] mp. 149°. ^{1}H NMR ($CDCl_3$: DMSO-d_6 9:1): δ 9.0 (s, 2H, NH_2), 8.0 (d, 2H, Ph-H), 6.9 (d, 2H, Ph-H), 3.9 (s, 3H, CH_3O-). MS (m/z): 167 (M^+, 100%), 151, 134.

4-Methylthiobenzamide, mp. 170-172° (from ethanol), lit.[7b] mp. 168°. ^{1}H NMR ($CDCl_3$:DMSO-d_6 9:1): δ 8.4 (s, 2H, NH_2), 7.9 (d, 2H, Ph-H), 2.4 (s, 3H, Me-). MS (m/z): 151 (M^+, 100%), 135, 118, 91, 60.

4-Dimethylaminothiobenzamide, mp. 170°, 203°, lit.[9a] 170°, 207°. ^{1}H NMR ($CDCl_3$: DMSO-d_6 9:1): δ 8.7 (s, 2H, NH_2), 7.8 (m, 2H, Ph-H), 6.7 (m, 2H, Ph-H), 3.1 (m, 6H, Me_2N-). MS (m/z): 180 (M^+, 100%), 164, 147, 105.

4-Trifluoromethylthiobenzamide, mp. 135-137° (from toluene), lit.[10] mp. 135°. ^{1}H NMR (DMSO-d_6): δ 7.5-7.0 (q, 4H, Ph-H), 3.5-4.0 (s, 2H, NH_2). MS (m/z): 205 (M^+, 100%), 189, 172, 145, 60.

4-Bromothiobenzamide, mp. 138-140° (from toluene), lit.[9b] 141.5°. ^{1}H NMR (DMSO-d_6): δ 9.8-9.5 (s, 2H, NH_2), 7.9-7.6 (m, 4H, Ph-H). MS (m/z): 217 (M^+ +2, 100%), 215 (M^+, 100%), 201, 199, 184, 182, 136, 120, 102, 60.

Phenylthioacetamide, mp. 96-97.5° (from ethanol), lit.[11] 96-96.5°. ^{1}H NMR (DMSO-d_6): δ 9.3 (s, 2H, NH_2), 7.3 (m, 5H, Ph-H), 3.3 (s, 2H, CH_2). MS (m/z): 151 (M^+, 100%), 135, 118, 92, 91, 60.

4-Chlorophenylthioacetamide, mp. 155-157° (from dioxane:water 9:1), lit.[9c] 128-129°. ^{1}H NMR ($CDCl_3$: DMSO-d_6 1:1): δ 7.2 (m, 4H, Ph-H), 6.7 (s, 2H, NH_2), 3.4 (s, 2H, CH_2). MS (m/z): 185 (M^+, 3%), 169, 125, 91, (100%).

4-Methoxyphenylthioacetamide, mp. 190-192° (from dioxane).[9d] ^{1}H NMR ($CDCl_3$: DMSO-d_6 1:1): δ 7.3 (d, 2H, Ph-H), 6.9 (d, 2H, Ph-H), 3.8 (s, 3H, CH_3O-), 3.5 (s, 2H, CH_2), 3.4 (s, 2H,NH_2). MS m/z): 181 (M^+, 30%), 165, 121 (100%), 107.

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SOLVENT EFFECT ON THE GOMBERG-BACHMANN-HEY ARYLATION OF PYRIDINE

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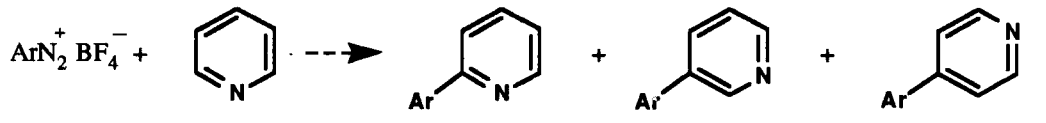
Polychlorinated (PCB) biphenyls are very stable materials of low flammability and are exceptionally persistent in the environment. This fact coupled with their carcinogenicity,[1] require that they be eliminated from several applications. Polychlorinated phenylpyridines may be considered as possible substitutes as they are less hydrophobic and more susceptible to biodegradation; indeed, the nitrogen should relatively easily be oxidized, protonated and methylated and should coordinate to metals ions. Among possible chloro derivatives of phenylpyridines, the 4-phenyl isomers seem to be most promising.



1 2 3 4

a) Ar = 4-$NO_2C_6H_4$ b) Ar = C_6H_5 c) Ar = 4-$EtOC_6H_4$