A Novel Method for the Preparation of 4,6-Diphenyl-2-pyridyl Sulfides

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The synthetic utility of 2-pyridyl sulfides was shown in several new applications, such as regiospecific carbon-carbon bond formation[1,2], preparation of olefins[3] and thiiranes[4], and applications as alkylating agents[5]. Two general methods for their preparation have been reported: the first involves the reactions of activated pyridines, e.g. *N*-oxides[6,7,8], 2-halopyridines[9], or lithium derivatives[10] with thiolate anions. The second method involves reactions of 2-mercaptopyridines with alkyl halides, under alkaline conditions[3] or phase transfer catalysis[11], or with 1-methyl-2-alkoxpyridinium salts, available from alcohols and 1-methyl-2-halopyridinium salts in the presence of triethylamine[12].

However, no generally useful procedure for the preparation of 2-pyridyl sulfides **5** from amines has hitherto been reported; it has only been briefly mentioned[13] that 4,6-diphenyl-5′-methyl-2,2′-bipyridyl sulfide may be obtained in 40% yield by thermal treatment of the 1-(5-methyl-2-pyridyl)-4,6-diphenyl-1,2-dihydropyridine-2-thione. This transformation is not successful in the case of the *N*-4-tolyl derivative; the 2-pyridyl function or a similar activating group on the *N*-substituent is necessary to facilitate this migration.

Previously, we have reported that the reaction of non-diazotizable amines **1** with 4,6-diphenyl-2*H*-pyran-2-thione **(2)** leads to the corresponding *N*-substituted 4,6-diphenyl-1,2-dihydropyridine-2-thiones **3** which are useful intermediates to achieve the conversion of the amino group into another functionality[14–17]. In this context, we report here a convenient two-step synthesis of 2-pyridyl sulfides **5** from amines **1** and 4,6-diphenyl-2*H*-pyran-2-thione **(2)**. The method involves the initial formation of pyridine-2-thiones **3** which, by heating at 170 °C under nitrogen, undergo a Chapman rearrangement to give the desired 2-pyridyl sulfide **5** in excellent yields (70–90%) (Method A). The method appears to be quite general; it proceeds satisfactorily for arylmethanamines, hetero analogs, and unsaturated aliphatic amines.

Unexpectally, compounds **5** are also obtained in good yields (69–79%) when a dry admixture of sodium methoxide and pyridinium iodide **4** is heated at 150–170 °C for 3 h (Method B). We believe that this conversion involves regiospecific nucleophilic attack of the methoxide anion on the *S*-methyl group of the pyridinium iodide **4** to give dimethyl ether and **3** which, under the reaction conditions, undergoes the above-mentioned rearrangement.

4,6-Diphenyl-2-pyridyl Sulfides 5; General Procedures:

Method A: from 1,2-dihydropyridine-2-thiones **3:** The 1,2-dihydropyridine-2-thione **3** (20 mmol) is heated in an oil-bath at 170 °C under nitrogen for 3 h. After cooling, the solid is dissolved in hot ethanol (100 ml) and the resultant solution treated with animal charcoal and concentrated to give a solid which recrystallizes from ethanol to give **5** as light yellow crystals.

Method B: from pyridinium iodides **4:** A dry mixture of pyridinium iodide **4** (10 mmol) and sodium methoxide (0.54 g, 10 mmol) is heated at 150–170 °C for about 3 h. After cooling, the solid remaining in the

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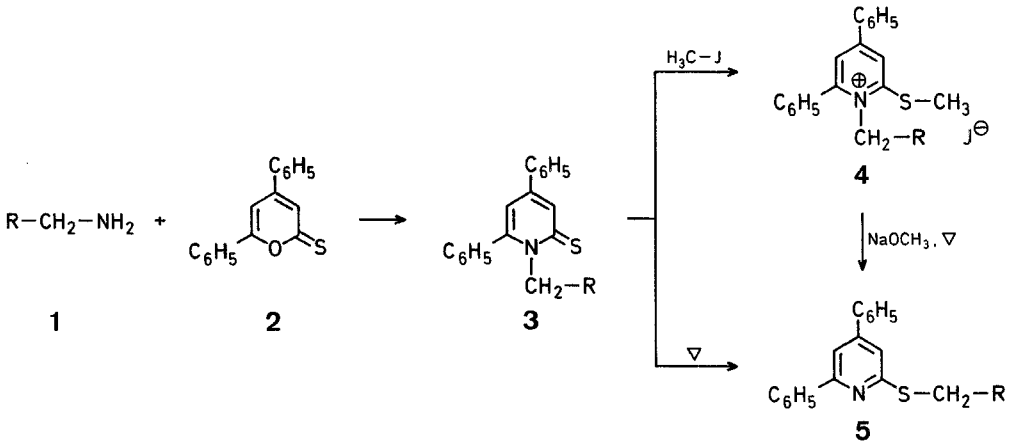
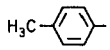
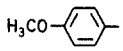
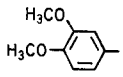


flask is treated with ether (75 ml). The inorganic salt is filtered off, the filtrate is dried with magnesium sulfate, and evaporated in vacuo to leave the crude product which is recrystallized from ethanol to give **5**.

Table. 4,6-Diphenyl-2-pyridyl Sulfides **5**

Product No.	R	Yield [%][a] by Method A	Yield [%][a] by Method B	m.p.[b] [°C]	Molecular formula[c] or Lit. m.p. [°C]	
5a		76	77	107–109°	107–109°[17]	
5b		75	68	106–108°	$C_{24}H_{18}ClNS$	(387.9)
5c		81	72	85–87°	$C_{25}H_{21}NS$	(367.5)
5d		87	75	84–86°	$C_{25}H_{21}NOS$	(383.5)
5e		90	79	110–112°	$C_{26}H_{23}NO_2S$	(414.2)
5f		70	69	95–96°	$C_{23}H_{18}N_2S$	(354.5)
5g	$H_2C{=}CH-$	70	—	62–64°	$C_{20}H_{17}NS$	(303.4)

[a] Yield of pure isolated product. The ^{1}H-N.M.R. spectra of all products **5** show a singlet at $\delta = 4.60$–4.65 ppm corresponding to S—CH_2—R.

[b] Not corrected.

[c] Satisfactory microanalyses obtained: C ±0.22, H ±0.13, N ±0.15, S ±0.33.

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