

Synthesis of 2-Methyl-4-quinolyl Isothiocyanate

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Received December 9, 2003

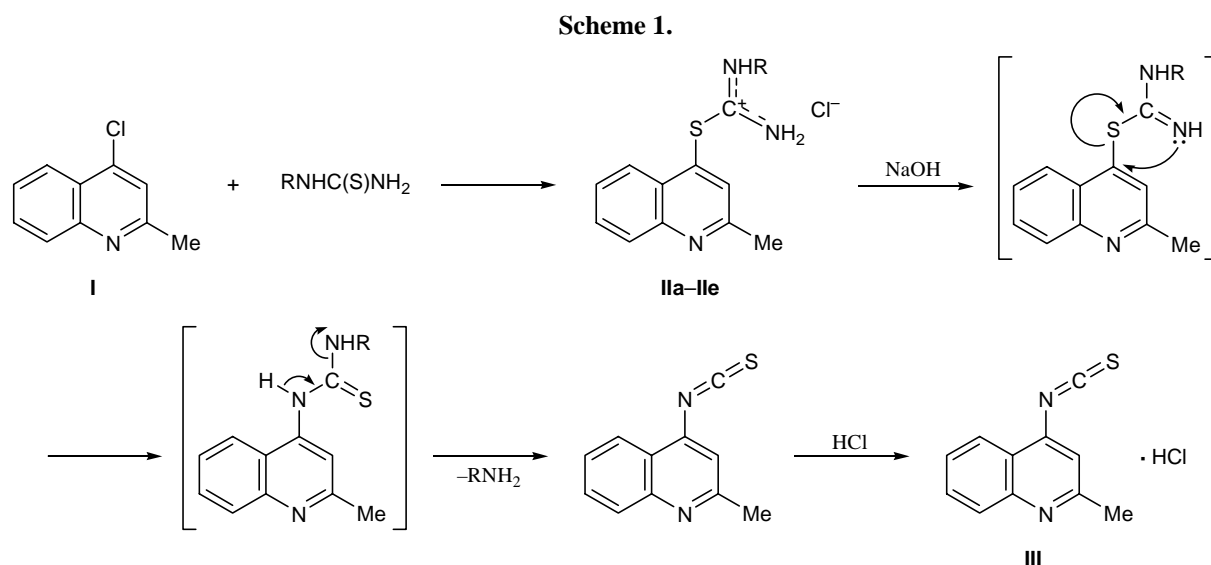
Abstract—A procedure has been developed for the synthesis of substituted 2-methylquinolin-4-ylthiuronium salts by reaction of 2-methyl-4-chloroquinoline with *N*-substituted thioureas. Alkaline hydrolysis of these salts yields 2-methyl-4-quinolyl isothiocyanate instead of the expected 2-methylquinoline-4-thiol.

In continuation of our studies on the synthesis of new quinoline derivatives, in the present work we examined reactions of 2-methyl-4-chloroquinoline [1] with substituted thioureas (thiourea, *N*-phenylthiourea, *N*-*o*- and -*p*-tolylthioureas, and *N*-*p*-ethoxyphenylthiourea) [2–4]. By heating the reactants at a ratio of 1 : 1.1 in anhydrous acetone we isolated the corresponding *S*-(2-methyl-4-quinolyl)thiuronium salts **IIa–IIe** in almost quantitative yields (Scheme 1). With a view to obtain 2-methylquinoline-4-thiol, salts **IIa–IIe** were subjected to alkaline hydrolysis. We previously showed that alkaline hydrolysis of 3-alkyl-, 3-allyl-, and 3-(3-chloro-2-butenyl)-2-methyl-4-quinolylthiuronium salts leads to the corresponding 3-substituted quinoline-4-thiols [5, 6]. However, the hydrolysis of salts **IIa–IIe** unexpectedly resulted in formation of

2-methyl-4-quinolyl isothiocyanate. Presumably, the reaction is accompanied by intramolecular nucleophilic substitution by analogy with the Smiles rearrangement [7–10]. *N*-Substituted *N'*-quinolylthioureas thus formed lose ammonia or aromatic amine molecule, yielding 2-methyl-4-quinolyl isothiocyanate (**III**) (Scheme 1).

EXPERIMENTAL

The ^1H NMR spectra were recorded on a Varian Mercury-300 spectrometer from solutions in $\text{DMSO-}d_6$. The IR spectra were measured on a UR-20 instrument from samples dispersed in mineral oil. The purity of the products was checked by TLC on Silufol UV-254 plates; development with iodine vapor. The



R = H (**a**), Ph (**b**), *o*-MeC₆H₄ (**c**), *p*-MeC₆H₄ (**d**), *p*-EtOC₆H₄ (**e**).

Yields, melting points, and elemental analyses of N-substituted S-(2-methylquinolin-4-yl)thiuronium chlorides **IIa–IIe**

Comp. no.	Yield, %	mp, °C (decomp.)	Found, %					Formula	Calculated, %				
			C	H	Cl	N	S		C	H	Cl	N	S
IIa	98	170–172	52.18	4.58	14.19	16.48	12.68	C ₁₁ H ₁₂ ClN ₃ S	52.07	4.73	14.00	16.57	12.62
IIb	95	184–185	61.72	4.98	10.56	12.83	9.84	C ₁₇ H ₁₆ ClN ₃ S	61.91	4.86	10.77	12.75	9.71
IIc	94	190–191	62.72	5.41	10.19	12.30	9.27	C ₁₈ H ₁₈ ClN ₃ S	62.88	5.24	10.33	12.22	9.32
IId	96	210–212	62.75	5.39	10.41	12.17	9.45	C ₁₈ H ₁₈ ClN ₃ S	62.88	5.24	10.33	12.22	9.32
IIe	95	205–206	60.90	5.51	9.70	11.31	8.49	C ₁₉ H ₂₀ ClN ₃ OS	61.04	5.35	9.50	11.24	8.57

yields and elemental analyses of compounds **IIa–IIe** are given in table.

N-Substituted S-(2-methyl-4-quinolyl)thiuronium chlorides IIa–IIe. A mixture of 1.775 g (0.01 mol) of 4-chloro-2-methylquinoline [1] and 0.013 mol of N-substituted thiourea [2] in 50 ml of anhydrous acetone was heated for 5 h on a water bath. The mixture was cooled, and the yellow crystals were filtered off and washed with anhydrous acetone.

2-Methyl-4-quinolyl isothiocyanate (III). An aqueous solution of 0.01 mol of thiuronium salt **IIa–IIe** was adjusted to pH 10 and was heated for 1.5 h on a water bath. After cooling, the precipitate was filtered off, washed with water, and recrystallized from aqueous alcohol (1:1). mp 160–161°C. Yield 80, 71, 85, 81, and 83% from compounds **IIa–IIe**, respectively. The filtrate was extracted with benzene, and the extract was evaporated to isolate the corresponding aromatic amines. Samples of **III** obtained from compounds **IIa–IIe** showed no depression of the melting point on mixing. *R_f* 0.70 (alcohol). IR spectrum, ν , cm⁻¹: 930–1250 (N=C=S). ¹H NMR spectrum, δ , ppm: 2.60 s (3H, CH₃), 7.02 s (1H, 3-H), 7.5–8.2 m (4H, H_{arom}). Found, %: N 14.07; S 16.11. C₁₁H₈N₂S. Calculated, %: N 14.00; S 16.00. Hydrochloride: mp 225°C (decomp.); picrate: mp 235°C. Complexes of **III** with CoCl₂ (blue) and CuCl₂ (yellow) in acetone were also synthesized; mp 255–260 and 215–220°C, respectively.

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