

Chemistry of Thienopyridines. X. Syntheses of Thieno[3,4-*b*]- and Thieno[3,4-*c*]pyridines (1)

L. H. Klemm, W. O. Johnson (2), and D. V. White (3)

Department of Chemistry, University of Oregon

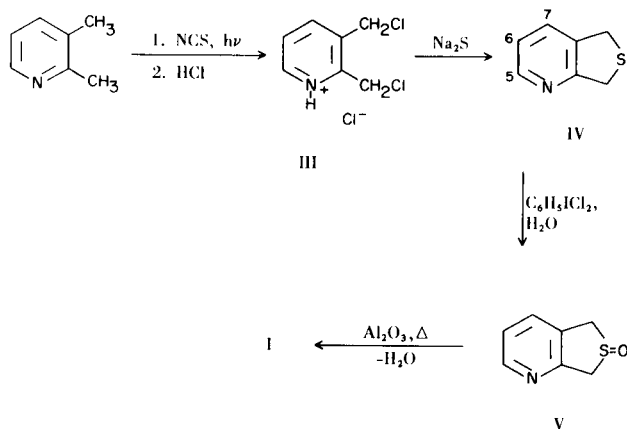
Sir:

Practical syntheses of four of the six possible isomeric thienopyridines have been reported recently (4-6). We now describe preparative four-step syntheses for the other two isomers, thieno[3,4-*b*]pyridine (I) and thieno[3,4-*c*]pyridine (II), previously unknown.



Starting materials were 2,3-dimethylpyridine and 3,4-dimethylpyridine, respectively. The procedure for I is outlined in Scheme I.

Scheme I



Ultraviolet irradiation by means of an Hanovia lamp (pyrex filter) of a stirred, refluxing solution of 2,3-dimethylpyridine and *N*-chlorosuccinimide in carbon tetrachloride (nitrogen atmosphere) was monitored by nmr in order to obtain a maximum yield of the bischloromethyl derivative, isolated as the hydrochloride salt III (77%), m.p. 147.5-148.5 dec., nmr (hexadeuterio-DMSO): singlets at δ 10.79

(1H NH⁺), 5.16 (2H, CH₂Cl at C-2), and 5.07 (2H, CH₂Cl at C-3); doublets of doublets for 1H each at 8.78 (H-6), 8.42 (H-4), and 7.82 (H-5); $J_{4,5} = 8$ Hz, $J_{4,6} = 1.8$, $J_{5,6} = 5.2$.

Anal. Calcd. for C₇H₈Cl₂N: C, 39.56; H, 3.79; Cl, 50.05; N, 6.59. Found: C, 39.70; H, 4.10; Cl, 49.94; N, 6.65.

Treatment of III with aqueous ethanolic sodium sulfide (nitrogen atmosphere) and chromatography of the organic product on Florisil gave IV, isolated as a liquid (59%); nmr (deuteriochloroform): singlets for 2H each at δ 4.26 (CH₂ α to N) and 4.20 (CH₂ β to N); doublets of doublets for 1H each at 8.40 (H-5), 7.50 (H-7), and 7.05 (H-6; $J_{5,6} = 5$ Hz, $J_{5,7} \approx 1.5$, $J_{6,7} = 7.5$).

Oxidation of IV was effected by means of iodobenzene dichloride (7) in aqueous acetonitrile containing triethylamine. Chromatography gave liquid sulfoxide V (56%); infrared band (chloroform) at 1030-1050 cm⁻¹ (very strong, sulfoxide); appropriate nmr spectrum.

Heating neutral alumina impregnated with V *in vacuo* (8) caused distillation of I as a yellow liquid (90%); uv max. (95% ethanol) at 224 nm (log $\epsilon = 4.27$), 293 (3.81), 296 (3.79, shoulder), 306 (3.88) 343 (3.46); nmr (deuteriochloroform): doublet of doublets for 1H each at δ 8.57 (H-5) and 6.90 (H-6; $J_{5,6} = 3.7$ Hz, $J_{5,7} = 1.8$, $J_{6,7} = 8.5$), multiplet at 8.02-7.78 (2H, H-3 and H-7), and a doublet at 7.66 (1H, H-1, $J_{1,3} = 3.2$ Hz). A picrate of I melted at 207.5-209°.

Anal. Calcd. for C₁₃H₈N₄O₇S: C, 42.86; H, 2.21; N, 15.38; S, 8.80. Found: C, 43.18; H, 2.27; N, 15.05; S, 8.55.

Similarly, from 3,4-dimethylpyridine were obtained (in turn) 3,4-bis-chloromethylpyridinium chloride [(67%), m.p. 157-159° dec. Found: C, 39.55; H, 3.77; Cl, 50.27; N, 6.57], 1,3-dihydrothieno[3,4-*c*]pyridine (83%), 1,3-dihydrothieno[3,4-*c*]pyridine 2-oxide [(67%); very strong infrared band (chloroform) at 1040-1055 cm⁻¹], and liquid II (37%). Appropriate nmr spectra were obtained for the intermediates.

Thienopyridine II showed uv max. (absolute ethanol) at 224 nm (log $\epsilon = 4.32$), 270 (3.35, shoulder), 280 (3.46), 291 (3.31), 342 (3.47); nmr (deuteriochloroform):

slightly broadened singlet at δ 9.12 (1H, H-4), two overlapping doublets for 2H total at *ca.* 8.04 (H-6) and 8.02 (H-1 or H-3), a doublet at 7.64 (1H, H-3 or H-1, $J_{1,3} = 3$ Hz), and a slightly split doublet at 7.38 (1H, H-7, $J_{6,7} = 6.5$ Hz). Compound II formed a picrate, m.p. 234-235° dec. Found: C, 42.76; H, 2.10; N, 15.22; S, 8.63.

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(2) Texaco Predoctoral Fellow, 1968-1969.

(3) Research Associate, 1969-.

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Eugene, Oregon 97403