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Isolation of 2-Chloro-5-methylpyridine from its Isomer 2-Chloro-3-methylpyridine by Formation of its Copper(II) Complex

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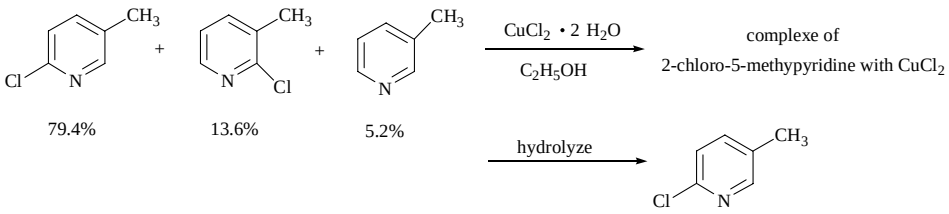
Abstract: 2-Chloro-5-methylpyridine can be effectively isolated from its isomer 2-chloro-3-methyl-pyridine in the form of Cu^{2+}complex. After hydrolyzing the complex, it can be obtained in more than 99.1% purity.

Keywords: Isolation, 2-chloro-5-methylpyridine.

2-Chloro-5-methylpyridine is an important intermediate for the preparation of biological active compounds, especially insecticides[1], *e.g.* imidacloprid[2], and is usually manufactured from 3-methylpyridine N-oxide. However, the manufacturing process also forms the by-products: 3-methylpyridine and its isomer 2-chloro-3-methylpyridine[3]. The properties of the isomers are similar, it is difficult to separate by ordinary methods, such as distillation.

Scheme 1



As we know, pyridine and its derivative usually can form the complex with the transition-metal ion, and the substituted groups in different position may affect the complex formation ability[4-6]. We have found that the crystalline complex of 2-chloro-5- methylpyridine can be formed easily when crude 2-chloro-5-methylpyridine is mixed with $CuCl_2 \cdot 2H_2O$ in absolute ethanol, the complex can be isolated from the mixture by filtration, and the other compounds remain in the solution. Finally, 2-chloro-5-methyl pyridine is obtained with over 99% purity after hydrolyzing the obtained complex. The total yield of pure product was 68.8% based on

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2-chloro-5-methylpyridine in the starting mixture. The overall courses can be described as **Scheme 1**.

Experimental

*Preparation of 2-chloro-5-methylpyridine complex of Cu **(II)**:* 12.0 g (0.096 mol) crude product[3] in 30 mL absolute ethanol was mixed with 5.0 g (0.029 mol) $CuCl_2 \cdot 2H_2O$ in 20 mL absolute ethanol in a round bottom flask, the blue precipitate appeared immediately. To the mixture, another 50 mL absolute ethanol was added, and refluxed for 15 minutes. The precipitate was turned from blue to dark violet. After suction filtration, the product was washed with absolute ethanol and dried, 10.5 g dark violet crystalline precipitate was got.

Hydrolysis of the complex: 4.0 g complex was added in 20 mL water, heated to reflux for 20 minutes, then 10 mL chloroform was added and refluxed for another 15 minutes. The reaction mixture was cooled to room temperature, the oily layer was separated, washed with 5% NaOH solution till it was colorless, then washed with water 10 mL×2. Chloroform was vaporized to give 2.5 g 2-chloro-5-methylpyridine (yield 96.2%, purity 99.1%).

Identification of the complex: ^{1}H-NMR and ^{13}C-NMR spectra of complex were recorded on VANCE DMX500. IR spectrum (cm^{-1}, KBr) of the complex was recorded on NEXUS 670 spectrometer. C, H, N analysis was obtained by using Eager 2000 elemental analyzer. Melting point determination was performed on XRC-1 melting-point apparatus. The complex was recrystallized in absolute ethanol, mp: 140℃(decomposed). Anal. Calcd. for $C_{12}H_{12}Cl_4N_2Cu$: C, 37.02; H, 3.08; N, 7.19. Found: C, 37.05; H, 3.39; N, 7.60%. IR (cm^{-1}, KBr): 3448, 3089, 3053, 3019, 1599, 1573, 1473, 1454, 1377, 1298, 1248, 1230, 1146, 1120, 1056, 841, 729, 675, 637, 505, 444. ^{1}H-NMR(DMSO-d_6, TMS, δ ppm): 2.380(s, 3H, CH_3), 7.770(s, 2H, H-3 and H-4), 9.024(s, 1H, H-6). ^{13}C-NMR(DMSO-d_6, TMS, δ ppm): 17.832, 126.112, 134.631, 140.207, 146.026, 148.044.

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