

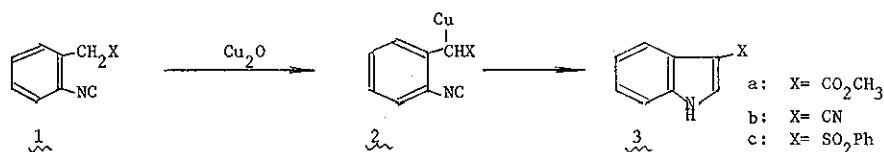
COPPER-CATALYZED CYCLIZATION OF o-TOLYL ISOCYANIDES

— A NEW SYNTHESIS OF INDOLES

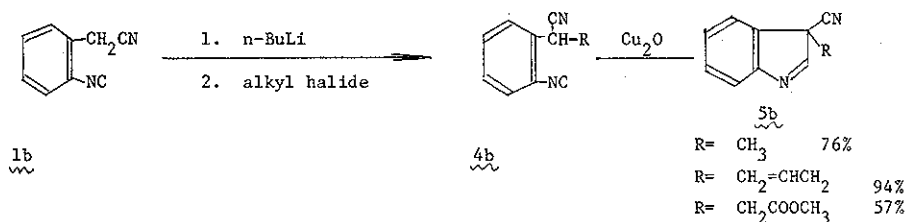
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A Cu_2O -catalyzed reaction of phenyl isocyanides having α -acidic hydrogens at the ortho-position producing indole derivatives was studied. o-Carbomethoxymethylphenyl isocyanide (1a), o-cyanomethylphenyl isocyanide (1b) and o-(phenylsulfonylmethyl)phenyl isocyanide (1c) were heated in benzene with a catalytic amount of Cu_2O to afford 3-carbomethoxyindole (3a, 92%; 55°C, 6 hr), 3-cyanoindole (3b, 86%; 55°C, 6 hr) and 3-phenylsulfonylindole (3c, 78%; 80°C, 10 hr) respectively.



The indole synthesis may be explained by a mechanism involving organocopper intermediate (2). Lithiation of 1b with n-BuLi at -78° followed by the reaction with alkyl halides furnished o-(α -cyanoalkyl)phenyl isocyanide (4b) in moderate yields. o-(α -Cyanoalkyl)phenyl isocyanides thus obtained were subjected to the Cu_2O -catalyzed cyclization reaction to give the corresponding 3-alkyl-3-cyano-3H-indoles in high yields.



Treatment of 1c with alkyl halides under phase-transfer reaction conditions [$\text{NaOH}/\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}/(\text{n-Bu})_4\text{NCl}$] gave directly 3-alkyl-3-phenylsulfonyl-3H-indoles in moderate yields via the alkylation and cyclization.