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COPPER-CATALYZED CYCLIZATION OF o-TOLYL ISOCYANIDES

—— A NEW SYNTHESIS OF INDOLES

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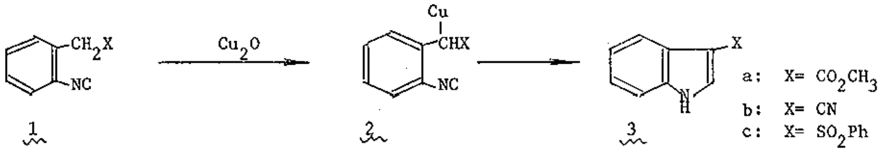
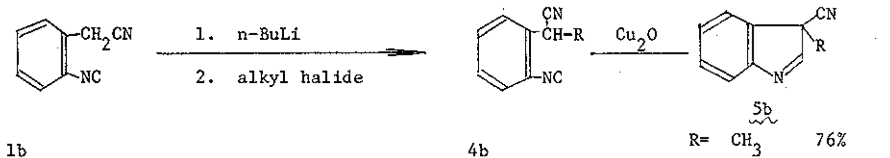
A Cu_2O-catalyzed reaction of phenyl isocyanides having α-acidic hydrogens at the ortho-position producing indole derivatives was studied. o-Carbomethoxymethylphenyl isocyanide(1a), o-cyanomethylphenyl isocyanide(1b) and o-(phenylsulfonylmethyl)phenyl isocyanide(1c) were heated in benzene with a catalytic 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.



a: X= CO_2CH_3
b: X= CN
c: X= SO_2Ph

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.



R= CH_3 76%
R= CH_2=$CHCH_2$ 94%
R= CH_2COOCH_3 57%

Treatment of 1c with alkyl halides under phase-transfer reaction conditions [$NaOH/CH_2Cl_2/H_2O/(n\text{-}Bu)_4NCl$] gave directly 3-alkyl-3-phenylsulfonyl-3H-indoles in moderate yields via the alkylation and cyclization.