HETEROCYCLE SYNTHESES USING o-LITHIOMETHYLPHENYL ISOCYANIDE INTERMEDIATES

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o-Lithiomethylphenyl isocyanide (1) is reacted with α,β-unsaturated ketones and aldehydes at -78° to produce o-(2-hydroxy-3-alkenyl)phenyl isocyanides (2) in high yields [e. g., o-(2-hydroxy-2,4-dimethyl-3-pentenyl)phenyl isocyanide (93%); o-(2-hydroxy-4-phenyl-3-butenyl)phenyl isocyanide (98%)]. Treatment of 2 with Lewis acid such as $BF_3.OEt_2$ and $ZnCl_2$ gives N-formyl-2-(1-alkenyl)-indolines (3) [e.g., N-formyl-2-methyl-2-(2-methyl-1-propenyl)indoline (80%); N-formyl-2-(2-styryl)-indoline (88%)]. Similarly, o-(2-hydroxy-2-arylalkyl)phenyl isocyanides (4), which are prepared by the reaction of 1 with aromatic ketones [e.g., o-(2-hydroxy-2-phenylpropyl)phenyl isocyanide (95%); o-(2-hydroxy-2-β-naphthylpropyl)phenyl isocyanide (∼100%)], are treated with $BF_3.OEt_2$ to afford N-formyl-2-alkyl-2-arylindolines (5) [e.g., N-formyl-2-methyl-2-phenylindoline (78%); N-formyl-2-methyl-2-β-naphthylindoline (70%)]. On the other hand, 1 reacts with α,β-unsaturated carboesters to give 1,4-addition products (6) [e.g., methyl 4-(o-isocyanophenyl)-3-methylbutyrate (81%); methyl 4-(o-isocyanophenyl)-3-propylbutyrate (∼100%)]. 6 is hydrolyzed by methanolic aq. HCl and then heated at 150∼180° to furnish benzocaprolactam (7) in moderate yield.
Finally, one-flask synthesis of 3-alkylindoles (8) starting with 1 is described, in which 1 generated at -78° is warmed up to room temperature and then anhydrous MgI_2 is added prior to treatment with alkyl halides [e.g., 3-allylindole (80%); 3-benzylindole (∼100%)].