

HETEROCYCLE SYNTHESIS USING *o*-METHYLPHENYL ISOCYANIDE

Yoshihiko Ito, Kazuhiro Kobayashi and Takeo Saegusa

Department of Synthetic Chemistry, Faculty of Engineering

Kyoto University, Yoshida, Kyoto

It has already been reported that *o*-tolyl isocyanide is treated with 2 equiv of lithium diisopropylamide (LDA) in diglyme at -78° to generate *o*-lithiomethylphenyl isocyanide (1) in an almost quantitative yield and that *o*-lithiomethylphenyl isocyanide is a versatile intermediate for preparation of indole derivatives. This paper describes some other elaborations of 1 leading to indole derivatives and related heterocycles. The *o*-lithiomethylphenyl isocyanide (1) was treated with isocyanate and isothiocyanate at -78° to produce *N*-substituted *o*-isocyanophenylacetamide (2) and *o*-isocyanophenylacetothioamide (3) in good yields, respectively [e.g., *N*-*n*-butyl *o*-isocyanophenylacetamide (70%): *N*-phenyl *o*-isocyanophenylacetothioamide (82%)]. Isocyanides 2 and 3 thus obtained were treated with 2 equiv of LDA at -78° and then allowed to warm up to room temperature to afford indole-3-carboxamide (4) and indole-3-thiocarboxamide (5) in moderate yields, after H_2O work up [e.g., indole-3-(*N*-*tert*-butylcarboxamide) (57%) : indole-3-(*N*-cyclohexyl thiocarboxamide)(60%)]. On the other hand, isocyanide (2) was heated with a catalytic amount of Cu_2O in benzene to afford 4 together with dihydrobenzodiazepinone (6), the ratio of 4 to 6 depending upon the substituent on amide nitrogen.

The *o*-lithiomethylphenyl isocyanide (1) was reacted with allyl carboxylate at -78° to produce *o*-(acylmethyl)phenyl isocyanide (7) in moderate yields [e.g., *o*-(acetylmethyl)phenyl isocyanide (48%) : *o*-(benzoylmethyl)phenyl isocyanide (95%)]. *o*-(Acylmethyl)phenyl isocyanide (7) was treated with a catalytic amount of Cu_2O to afford 3-acylindoles in good yields [e.g., 3-butyrylindole (71%) : 3-benzoylindole (80%)].

Selective lithiations at the methyl groups of 2,4-xylyl isocyanide and 2,6-xylyl isocyanide and their elaboration to synthesize 3,5-disubstituted indole and 3,7-disubstituted indole will be also mentioned.