SYNTHESIS OF 1H-INDAZOLYL-3-ACETIC ACID DERIVATIVES

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As a part of our studies on the synthetic auxins, convenient synthesis of 1H-indazolyl-3-acetic acid (IDA) derivatives were investigated. Especially 5-chloro-IDA and its ester were evaluated to be effective plant growth regulators by another groups.

(A) Cyclization of 2-amino-5-chlorophenylsuccinic acid by diazotization easily carried out to give 5-chloro-IDA accompanied with decarboxylation in 75% yield.

(B) One step synthesis of 3H-indazole was studied as follows. Starting diazoester and benzyne were obtained from a mixed solution of anthranilic acid and diethyl aspartate in THF-ether by diazotization simultaneously. Then, 1,3-dipolar cycloaddition of the diazoester to the benzyne gave ethyl 3-ethoxycarbonyl-3H-indazolyl-3-acetate in 70% yield. Transformation of 3H-indazole to 1H-indazole were readily accompolished in 90% yield by acid hydrolysis followed by decarboxylation.

(C) β-(o-Nitrophenyl)-β-alanin derivatives were converted to IDA derivatives in high yield under mild reductive conditions using hydrazine hydrate as hydrogene carrier over Raney Ni or Al powder in aqueous NaOH.

The tird method should be a widely applicable and useful synthetic procedure of indazoles in comparison with known methods.