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REACTIONS OF ORGANIC ANIONS. XVII[x]. CATALYTIC ALKYLATION OF REISSERT COMPOUND IN AQUEOUS MEDIUM.

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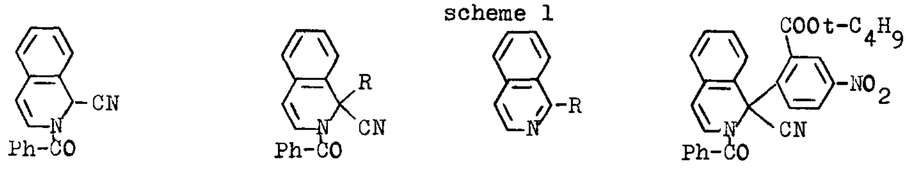
In 1952 Boekelheide (1) showed that Reissert compound (N-benzoyl-1,2-dihydroisoquinaldonitrile, I) when treated with phenyllithium at -20° gave the corresponding anion which reacted with alkyl halides to give 1-alkylderivatives (II). The products formed when subjected to alkaline hydrolysis, yielded the corresponding substituted isoquinolines (III) (see scheme 1). The latter are important intermediates in the synthesis of some alkaloids.

Recently, several authors have claimed an improved method for generating the anion from Reissert compound by use of sodium hydride in DMF at room temp. instead of PhLi at -20° (2). The new procedure is simpler and gives better yields as compared with the Boekelheide's method.

scheme 1



I II III IV

This prompts us to report our results on the catalytic alkylation of Reissert compound (I) in the presence of aqueous NaOH and triethylbenzylammonium (TEBA) chloride. As we have shown recently phenylacetonitrile and its derivatives may be alkylated with unsubstituted and substituted alkyl halides in the presence of aqueous NaOH and the catalyst (3). We expected that

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[x] Part XVI see preceding paper

Reissert compound, which also contained the Ar-CH-CN system, should be able to form the anion under such conditions. Actually, alkyl bromides and benzyl chloride were found to react exothermically with I in the presence of a 50% aqueous NaOH and catalytic amount (0.01 mole per mole I) of TEBA chloride, without any organic solvent used, to give the corresponding 1-alkyl-N-benzoyl-1,2-dihydroisoquinaldonitriles (II) in high yields. Since Reissert compound easily undergoes hydrolysis, the reaction must be carried out with external cooling to maintain 25°-30°.

As an example, from 6.5 g (0.025 mole) I, 4.5 g benzyl chloride, 10 ml 50% aqueous NaOH and 0.05 g TEBA chloride, after stirring at 25°-30° for 2 hours, 6.8 g (78%) N-benzoyl-1-benzyl-1,2-dihydroisoquinaldonitrile (m.p. 129° from methanol) was obtained. Other II obtained by this method were (R, yield, m.p.): C_2H_5, 76%, 103°; n-C_3H_7, 82%, 120°; n-C_4H_9, 78%, 107°.

Under the same conditions, the reaction may be carried out with p-chloronitrobenzene (some benzene is necessary for dissolving the substrates) to yield N-benzoyl-1-(p-nitrophenyl)-1,2-dihydroisoquinaldonitrile which, after alkaline hydrolysis, gave 1-(p-nitrophenyl)isoquinoline m.p. 155°, lit.(4) m.p. 155°.

Similarly from t-butyl 2-chloro-5-nitrobenzoate and I N-benzoyl-1-(4-nitro-2-carbobutoxyphenyl)-1,2-dihydroisoquinaldonitrile (IV) (yield 46%, m.p. 166°) was obtained.

All compounds give satisfactory elemental analysis.

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