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REACTIONS OF ORGANIC ANIONS. XLII. CATALYTIC ALKYLATION OF S-PHENYLTHIOGLYCOLONITRILE IN AQUEOUS MEDIUM*

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One of the most convenient method for performing alkylation of some C-H acids seems to be the catalytic one which consists in two phase reaction with aqueous 50 % NaOH and quaternary ammonium catalyst as a basic agent.

So far this method has been applied for alkylation of arylacetonitriles[1], cyclopentadiene hydrocarbons[2] and ketones[3]. However aliphatic nitriles that do not contain additional activating substituents generally can not be alkylated in these conditions.

Many observations as well as theoretical considerations indicate that divalent sulfur atom has significant effect stabilizing the negative charge on α-carbon atom by participation of non-occupied 3-d orbitals[4]. These proprieties are becoming of great importance in synthetic organic chemistry e.g. elegant method for "nucleophilic acylation" with 2-lithium derivatives of 1,3-dithianes[5], chemistry of sulfur ylides[6] etc. Owing of this phenomena it was possible to generate chlorophenylothiocarbene by action of aqueous NaOH in the presence of triethylbenzylammonium chloride (TEBA) on phenyldichloromethyl sulfide as we reported previously[7].

In this paper we would like to present another example of utilization of

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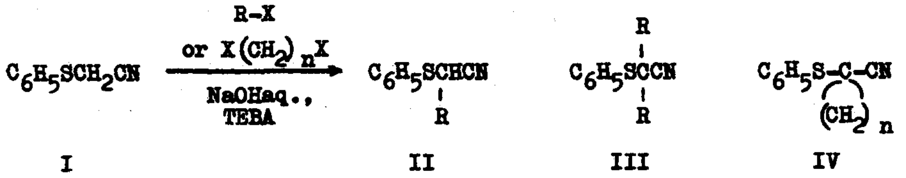
this effect in synthesis. Stabilization of the carbanion by divalent sulfur makes the acidity of S-phenylthioglycolonitrile (I) greatly enhanced as compared with acetonitrile itself and it is possible to alkylate(I) in the presence of aqueous NaOH and TEBA.

Alkyl bromides like ethylbromide or butylbromide react easily in these conditions with (I) giving rise to the formation of corresponding alkylated derivatives (II): R = C_2H_5 (IIa), yield 80 %, b.p. 135/10, R = n-C_4H_9 (IIb), yield 82 %, b.p. 112/0.3 . Also benzyl and allyl chlorides are good alkylating agents for (I).

Extend of side reaction - dialkylation of I is considerably lower as compared with the case of phenylacetonitrile. However using excess of alkylating agent makes it possible to obtain dialkylated product (III) with high yield.

Thus, for example the following dialkylated nitriles (III) were simply obtained: R = CH_3 (IIIa), 75 %; b.p. 117°/9; R = $CH_2{=}CHCH_2$ (IIIb), 80 %; b.p. 111°/0.4



It is worth to stress that contrary to the primary alkyl halides the secondary bromides e.g. iso-propylbromide and even very reactive benzhydryl chloride do not form in these conditions alkylated products. This is probably caused by great steric hindrance created by bulky S atom particulary being increased by sharing of carbanion's electron pair that is partially delocalized on sulfur 3d orbitals.

This effect can be also considered for explanation relatively high selectivity in respect of mono-versus dialkylation.

Alkyl dihalides $X(CH_2)_nX$ also react in these conditions with I yielding two main type of products: haloalkylderivatives e.g. II R = $(CH_2)_nCl$, n = 3, 39 %; b.p. 153/0.6 and cyclic nitriles IV. Yields of these nitriles although sometimes lower then of the corresponding phenylacetonitrile derivatives are quite satisfactory(n = 2, 47 %; b.p. 112°/0.5; n = 4, 69 %; b.p. 120/0.3; n = 5, 50 %; b.p. 135/0.5; m.p. 35°)

The following experiment can serve as an illustration of the method under consideration.

S-Phenylthioglycolonitrile (7.5 g, 0.05 mole), benzyl chloride (14.4 g, 0.11 mole), 50 % aqueous NaOH (20 ml), TEBA chloride (0.3 g) were stirred vigorously under nitrogen. After an exothermic reaction ceased the mixture was stirred for two h., diluted with water, product (III, R = $C_6H_5CH_2$) filtered and cristalized from methanol, m.p. 152°, 13.5 g; 82 % .

All compounds described in this work have NMR spectra in agreement with their structure and correct elemental analysis; their IR spectra shoved rather strong absorption band at 2230-2240 cm^{-1} (-CN) contrary to the phenoxyacetonitrile and its derivatives[8]. The nitriles II - IV can be hydrolysed in alkaline medium with the formation of corresponding carboxylic acid e.g. from IV (n = 2) 97 %, m.p. 109°;(n = 5) 89 %, m.p. 76° . Partial hydrolysis in acidic conditions leads to the formation of amides e.g. from II, R = C_2H_5, m.p. 118°, R = $C_6H_5CH_2$, m.p. 132°.

Oxidation of nitriles II-IV with peracetic acid or hydrogen peroxide leads to the formation of corresponding sulfones, e.g. from III R = CH_3, m.p. 105°; from IV n = 2, m.p. 88°; n = 5, m.p. 130°.

Participation of sulfur d-orbitals is critical for the possibility of performing such kind of alkylation. Phenoxyacetonitrile for example can not be succesfully alkylated nor in catalytic conditions, neither in the presence of sodium amide in liquid ammonia.

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