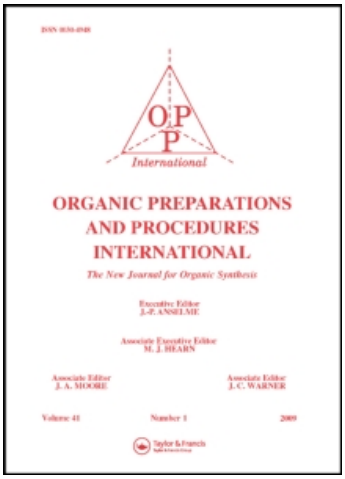

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A SIMPLE PROCEDURE FOR THE PREPARATION OF PURE MONOALKYL PHENYLACETONITRILES†

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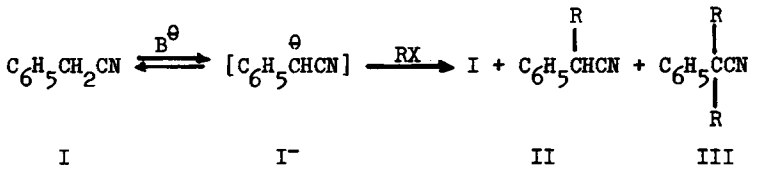
Alkyl derivatives of phenylacetonitrile (II) are conveniently prepared by reaction of phenylacetonitrile anion (I^-) with alkyl halides.[1] Although the yields of this reaction are usually high, the products are often contaminated with variable amounts of the starting nitrile (I) and the dialkyl derivatives (III).



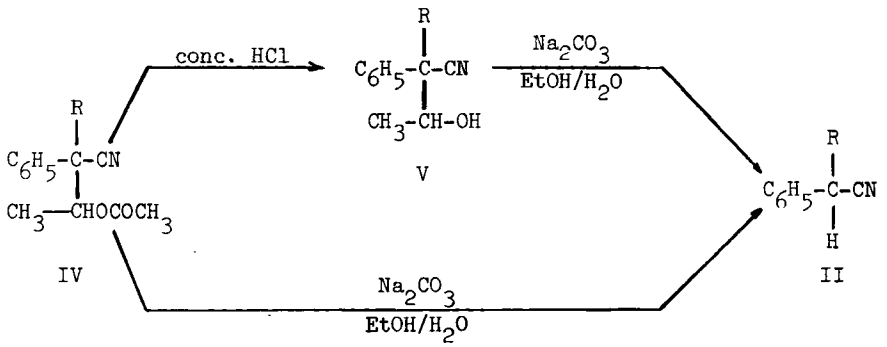
I I^- II III

For this reason, the preparation of pure II is often a difficult task, particularly when R are lower aliphatic substituents (CH_3, C_2H_5, CH_2=$CHCH_2$, etc.). Since in these cases the differences in boiling points are small, these compounds can only be separated by preparative GLC.

Among a variety of base-solvent systems employed for the alkylation of I, the most convenient and efficient is the so-called catalytic two-phase (CTP) system,[2,3] in which aqueous sodium hydroxide in the presence of tetraalkylammonium salt is used as the base for the generation of the carbanions. Although these conditions offer the best selectivity for the alkylation of I, small amounts of dialkyl derivatives (III) are still produced, which together with unchanged I contaminate the product. Although phenylacetoni-

trile (I) can be easily removed from the mixture by condensation with benzaldehyde, III free of II cannot be obtained by chemical means. Some contamination of II by III usually does not interfere when II is used as a starting material in further carbanion condensation reactions; indeed III cannot for a α-cyano carbanion and is usually less reactive in other reactions involving the cyano function. However, for many purposes it is essential to have the pure II in hand. Thus, we now describe a relatively simple and efficient method for preparation of pure II.

We have recently found[4] that II reacts easily under CTP conditions with vinyl acetate, giving acetoxynitriles IV. The ester function in these compounds is easily hydrolyzed by acids affording the corresponding hydroxynitriles V. These in turn when treated with weak base undergo retroaldol cleavage to II and acetaldehyde. More conveniently, II is prepared in one-step when IV is treated directly with weak base.



R = CH_3, C_2H_5, CH_2=$CHCH_2$

Thus, when a mixture of II and III is treated with vinyl acetate under CTP conditions, only II forms the adducts IV which can be easily separated by distillation.[5] Subsequent hydrolysis and retroaldol cleavage with sodium carbonate-ethanol/water leads to II, free of any contaminations (see Table).

The overall yields of II based on both steps, are in the range of 55-65%.

TABLE. Data on Conversion of IV to II

R	Yield of II (%)	Overall yield of II (based on both steps %)	Bp. of II (°C/mmHg) Obs.	Lit.
CH_3	88	55	112-114/13	90-91/5.5[6]
CH_3CH_2	90	64	109-111/10	102-104/7[3]
CH_2=$CHCH_2$	86	60	133-135/14	134-136/16[7]

Due to the availability of the starting materials and simplicity of the procedure, this method is highly recommended for the preparation of pure II.

EXPERIMENTAL[8]

Preparation of IV.- The crude reaction mixture, after alkylation of I with methyl, ethyl, allyl, bromide or allyl chloride, was stirred with benzaldehyde to condense unreacted I,[3] then distilled. The resulting mixture of II and III was checked by GLC[9] and treated with vinyl acetate in the CTP system.[4] The products (IV) were than purified by fractional distillation, their purity was confirmed by GLC:[10] 2-methyl-2-phenyl-3-acetoxybutyronitrile (IV, R = CH_3), bp. 102-105°/0.2 mmHg lit.[4] bp. 146-147°/8 mmHg, yield 63%; 2-ethyl-2-phenyl-3-acetoxybutyronitrile (IV, R = C_2H_5), bp. 100-104°/0.3 mmHg, lit.[4] bp. 156-158°/12 mmHg, yield 71%; 2-allyl-2-phenyl-3-acetoxybutyronitrile (IV, R = CH_2=$CHCH_2$), bp. 154-159°/15 mmHg, mp. 67-72° (hexane, mixture of diastereoisomers), yield 70%; NMR (δ, ppm): 1.07 d, 1.33 d, J = 6.5 Hz, 3H ($\underline{CH_3}$-CH); 1.78 s, 2.10 s, 3H (CH_3CO); 2.5-2.9 m, 2H ($\underline{CH_2}CH=CH_2$); 4.8-5.7 m, 4H (HC-O, $CH=CH_2$); 7.2-7,5 m, 5 H (C_6H_5); IR (cm^{-1}, in KBr): ν_{CN}=2253 (w), ν_{CO}=1740 (s).

Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.1; H, 7.0; N, 5.75.

Found: C, 74.3; H, 6.95; N, 5.75.

2-Methyl-2-phenyl-3-hydroxybutyronitrile (V, R = CH_3).- The adduct (IV, R = CH_3), 13.0 g (0.06 mole) and 40 ml conc. hydrochloric acid were refluxed for 2 hrs. The mixture was diluted with water (100 ml), extracted with benzene (3 x 20 ml). The combined organic extract was throughly washed with water to remove acetic acid, dried ($MgSO_4$) and the solvent was evaporated. The residue was analyzed by GLC[11] revealed the presence of alcohol (V, R = CH_3), unreacted IV (R = CH_3, ~12%), the nitrile (II, R = CH_3, ~2%) and traces of other products. In order to complete the hydrolysis,[12] the mixture was again treated with conc. hydrochloric acid in identical fashion to the first step. The residue isolated from the second stage hydrolysis was distilled to give V (R = CH_3), bp. 144-146°/6 mmHg (mixture of diastereoisomers), 8.0 g (76%), purity ~95% (by GLC[11]). NMR (δ, ppm): 1.05 d, 1.17 d, J = 6 Hz, 3H (CH_3-CH); 1.61 s, 1.71 s, 3H (CH_3); 3.71 s, 1H (OH); 3.94 q, J = 6 Hz, 1H (-CH); 7.16-7.52 m, 5H (C_6H_5); IR (cm^{-1}, film): ν_{CN}= 2254, ν_{OH}=3490.

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.4; H, 7.4; N, 8.0.

Found: C, 74.9; H, 7.4; N, 7.9.

Treating this alcohol with sodium carbonate-ethanol/water mixture as described below gave the nitrile (II, R = CH_3) in nearly quantitative yield.

Hydrolytic Cleavage of IV.- The adduct (IV, 0.1 mole), sodium carbonate (13.8 g, 0.13 mole), water (60 ml), and ethanol (120 ml) were refluxed for 3-5 hrs; the progress of the reaction was monitored by GLC.[10] After completion of the hydrolysis, ethanol was distilled from the mixture. The residue was diluted with water, extracted with benzene, the extract was washed with saturated aqueous NaCl, dried over $MgSO_4$ and distilled to

give pure II, at least 99% by GLC analysis (Table).[9]

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5. If starting mixture contains small amount of I (∿10%), the pure II can be isolated by this method as well.
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8. The NMR spectra were determined in CCl_4 on Jeol JNH-100H spectrometer at 100 MHz (TMS as an internal standard). The IR spectra were obtained using UR-10 Zeiss-Jena spectrophotometer. GLC analysis were performed on a Chrom-4 instrument, column A: 10% DEGS on Sterchamol, column B: 5% silicone oil OV-17 on Kieselgur/TMCS, column C: 5% silicone oil XE-60 on Kieselgur/TMCS. Bps. and mps. (taken in a capilary tube) are uncorrected.
9. The mixture after alkylation with methyl bromide was analyzed on column A, the other products on column B.
10. Column B.

11. Column C.

12. Less satisfactory result was obtained when acetic acid was distilled during the hydrolysis. Therefore, a two-stage hydrolysis procedure was devised to remove all acetic acid which could participate in the hydrolysis equilibrium.

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