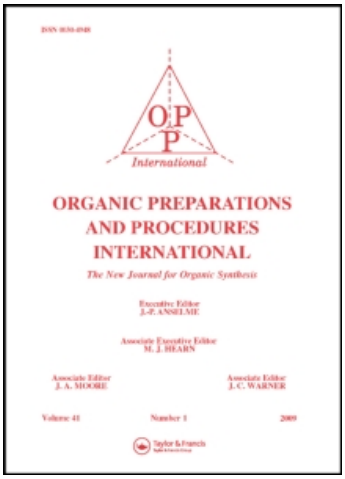

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SYNTHESIS OF PURE ARYLKETONE CYANOHYDRINS AND ARYLKETONES FROM AROMATIC ALDEHYDES

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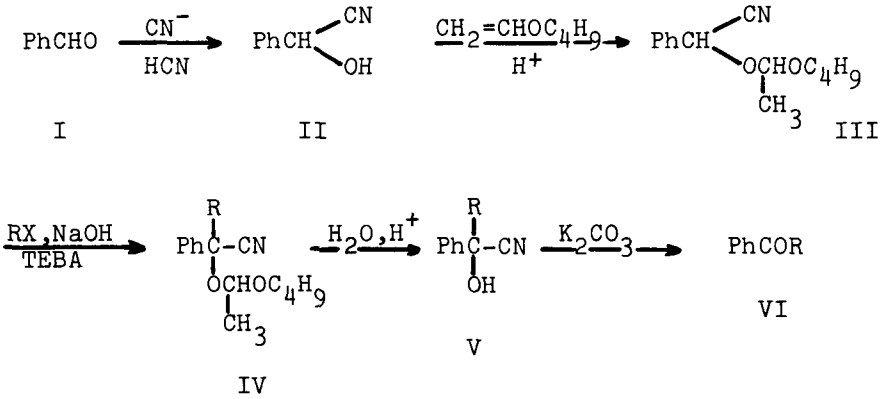
Although arylketone cyanohydrins are useful intermediates in organic synthesis,[1] the difficulties of direct preparative methods[2] have precluded their isolation in pure form. We now report a simple general method for the synthesis of aromatic ketones and the corresponding cyanohydrins from benzaldehyde.

Benzaldehyde cyanohydrin readily adds to vinyl ethers to give stable mixed acetals(III), which can be smoothly alkylated under basic conditions to the acetals of corresponding ketone cyanohydrins (IV). The alkylation is conveniently carried out in the presence of aqueous sodium hydroxide and triethylbenzylammonium chloride (TEBA) as a catalyst. Similar conditions were previously successful for the alkylation of



many C-H acids[3] as well as for some other reactions involving carbanions.[4] Although very stable toward alkali, these acetals (IV) are hydrolyzed rapidly in the presence of dil. hydrochloric acid to the cyanohydrins (V). The latter which are in turn quite stable to acids, are extremely sensitive to alkaline agents and decompose rapidly to corresponding ketones.

Thus, the reaction sequence described above offers a convenient path to pure cyanohydrins of arylketones even for difficultly accessible ones such as phenacyl bromide cyanohydrin. The method is also attractive for the synthesis of arylketones which are otherwise difficult to obtain; for example, using this method we have obtained pure allylphenylketone, which had previously eluded preparation.[5] The direct synthesis of ketones from benzaldehyde does not require purification of the intermediates II, IV and V.

EXPERIMENTAL[6]

α-(α-Butoxyethoxy)phenylacetonitrile (III). - Benzaldehyde (26.5 g, 0.25 mole), sodium cyanide (12.3 g, 0.25 mole) and 50 ml of water were mixed in a flask and then 250 ml of saturated aqueous $NaHSO_3$ was added during 15 min. with vigorous stirring and ice-cooling. The organic layer was separated and dried over $MgSO_4$ for 15 min. The resulting cyanohydrin was then treated with 3 drops of conc. HCl and 36 g (0.36 mole) of butylvinyl ether was added dropwise. The mixture was allowed to stand overnight at room temp., then washed with aqueous K_2CO_3 and distilled, yielding 40.8 g (70%) of

III, bp. 104-110°/0.4 mm, n_D^{20} 1.4857.

Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.2; H, 8.2
Found: C, 72.3; H, 8.3.

The NMR spectrums showed that the product to be an approximately 1:1 mixture of two isomers: δ H_α 5.3 and 5.4 ppm (1H), δ OCHO 4.8 and 5.0 ppm (two partly overlaping quartets, J = 5 Hz). The IR spectrum showed no C≡N absorption band as it is the case with many other α-cyanobenzyl ethers.

Allylphenylketone cyanohydrin (V, R = allyl). - Acetal III (9.3 g, 0.04 mole), allyl chloride (9.2 g, 0.12 mole), 50% NaOH (25 ml) and TEBA (0.22 g) were stirred for 2 hrs. at 50°. The mixture was diluted with water, the organic layer was separated, poured into 60 ml of 5% HCl and boiled for 5 min. After cooling, the product was extracted with benzene, dried over $MgSO_4$ and distilled, yielding 5.2 g (75%) of allylphenylketone cyanohydrin, bp. 100-102°/0.4 mm; n_D^{20} = 1.5286; NMR (δ, ppm): 2.6 (d, 2H, J = 6.5 Hz), 4.1 (1H), 4.85-5.2 (m, 2H), 5.3-6.0 (m, 1H), 7.1-7.5 (m, 5H); IR (cm^{-1}, film): ν_{CN} = 2249 (w), ν_{CH} = 3425 (s).

Anal. Calcd for $C_{11}H_{11}NO$: C, 76.3; H, 6.1; N, 8.1
Found: C, 76.5; H, 5.9; N, 8.0.

The following cyanohydrins were prepared similarly[7] from corresponding alkyl bromides.

Propiophenone cyanohydrin. - Yield 81%; bp. 94-96°/0.4 mm; n_D^{20} = 1.5194; NMR (δ, ppm): 0.9 (t, 3H, J = 7.5 Hz), 1.9 (q, 2H, J = 7.5 Hz), 4.4 (1H), 7.2-7.5 (5H); IR (cm^{-1}, film): ν_{CH} = 2247 (w), ν_{CH} = 3430 (s).

Anal. Calcd for $C_{10}H_{11}NO$: C, 74.5; H, 6.8; N, 8.4
Found: C, 74.2; H, 7.1; N, 8.7.

Butyrophenone cyanohydrin. - Yield 71%; bp. 101-103°/0.4 mm; n_D^{20} = 1.5135; NMR (δ, ppm) 0.7-2.1 (m, 7H), 4.15 (1H), 7.1-7.5 (m, 5H); IR (cm^{-1}, film): ν_{CH} = 2250 (w), ν_{CH} = 3440 (s).

Anal. Calcd for $C_{11}H_{13}NO$: C, 75.4; H, 7.4; N, 8.0
Found: C, 75.8; H, 7.1; N, 7.9.

Phenacyl bromide cyanohydrin. - Yield 73%; mp. 81° (from CCl_4); NMR (δ, ppm): 3.6 (d, 1H, J = 11 Hz), 3.65 (d, 1H, J = 11 Hz), 4.0 (1H), 7.1-7.5 (m, 5H); IR (cm^{-1}, in KBr): ν_{CN} = 2258 (w), ν_{CH} = 3440 (s).

Anal. Calcd for C_9H_8NOBr: C, 47.8; H, 3.5; N, 6.2
Found: C, 47.7; H, 3.8; N, 6.0.

Allylphenylketone. - Allylphenylketone cyanohydrin (3.5 g, 0.02 mole) was dissolved in 10 ml of methanol and poured into 50 ml of 5% K_2CO_3.[8] The mixture was shaken for 3 min. and extracted with benzene. The extract was dried over $MgSO_4$ and solvent was evaporated, yielding 2.95 g (100%) of allylphenylketone, bp. 52°/0.2 mm, n_D^{20} = 1.5410. NMR (δ, ppm): H_o, 7.9-8.2 (m, 2H); $H_{m,p}$, 7.2-7.8 (m, 3H); H_α, 3.7 (q, 2H, J^2_{H-H} = 6 Hz, J^3_{H-H} = 1 Hz); H_β, 5.8-6.5 (m, 1H); H_σ, 5.0-5.4 (m, 2H). IR (cm^{-1}, film): $\nu_{C=C}$ = 1648 (m), $\nu_{C=C}$ = 1690 (s).

Anal. Calcd for $C_{10}H_{10}O$: C, 82.2; H, 6.7
Found: C, 82.2; H, 6.8.

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5. The preparation of allylphenylketone have been described by Yu. K. Yur'ev [Zh. Obshch. Khim., 26, 3194 (1956)] and I. A. Favorskaya [Zh. Org. Khim., 4, 368 (1968)] but the reported properties of the compound are different from those obtained by us. Probably, the authors have obtained a mixture of isomeric α,β-unsaturated ketones instead of allylphenylketone.
6. The NMR spectra were determined in CCl_4 on JEOL C60H instrument. The IR spectra were obtained using UR-10 Zeiss-Jena recording spectrophotometer. Bp. and mp. (taken in a capillary tube) are not corrected.
7. If alkylation proceeds slowly, the addition of 5 ml of DMSO is recommended.
8. Stronger bases cause rapid isomerization with formation of two stereoisomers of phenylpropenylketone.

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