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OXIDATIVE DECYANATION OF PHENYLACETONITRILES WITH MOLECULAR OXYGEN IN AQUEOUS MEDIUM

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The alkylation of phenylacetonitrile (1) followed by the oxidative decyanation using molecular oxygen in aqueous alkali gave alkyl phenyl ketones (3).

The variety of reactions which the cyano group facilitates has stimulated the search for mild and efficient methods for its transformation into other functionalities, most notably the oxo group. Watt and co-workers developed a procedure of oxidative decyanation using molecular oxygen.1) However, the experimental procedure requires strictly anhydrous conditions and low temperature (-78°C) for the generation of carbanions. On the other hand, organic synthesis including the C-C bond formation in aqueous medium is one of the most attractive subjects.2) However, the system in aqueous medium places many restrictions on the C-C bond formation and the transformation into other functionalities.

Considering the above problems in mind, we have previously reported the utility of cyanomethyl dithiocarbamate as a reagent for ketone synthesis.3) In consequence of further investigation on oxidative decyanation, we found that direct oxygenation of phenylacetonitriles with molecular oxygen was achieved in aqueous medium. Accordingly, we wish to report here convenient ketone synthesis via the monoalkylation followed by oxidative decyanation using molecular oxygen starting from phenylacetonitrile.

The following is a general experimental procedure.

a) Alkylation:

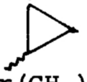
To a mixture of 5 mmol of phenylacetonitrile (1) in 2 ml of benzene and catalytic amount of $n\text{-}Bu_4N^+I^-$ (TBA) or $PhCH_2N^+Et_3Cl^-$ (TEBA) in 5 ml of 50% aq. NaOH was added 5 mmol of alkyl halide at room temperature under a nitrogen atmosphere. The reaction mixture was vigorously stirred for 10 hr and extracted with ether, and the ethereal solution was dried and concentrated under reduced pressure. The crude product was distilled or chromatographed to afford monoalkylated phenylacetonitrile (2) (Table 1).

b) Oxygenation (Oxidative decyanation):

Oxygen gas was bubbled with vigorous stirring into a mixture of 5 mmol of 2 in 2 ml of benzene and catalytic amount of TBA or TEBA in 5 ml of 50% aq. NaOH at room temperature for 24 hr. The reaction mixture was extracted with ether, and the ethereal solution was dried and concentrated. The crude product was chromatographed or recrystallized to afford alkyl phenyl ketone (3) (Table 1).

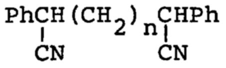
1 2 3

Table 1. Alkylation and Oxidative Decyanation[4)]

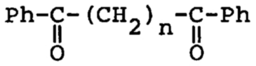
	RX	2,Yield%	R'	3,Yield%
a	$CH_3(CH_2)_5Br$	94	$CH_3(CH_2)_5$	83(79)[a)]
b	CH_3CH_2I	90	CH_3CH_2	78
c	$Cl(CH_2)_3Br$	95		82
d	$\genfrac{}{}{0pt}{}{Br}{CH_3}{>}CHCH_2CH_2Br$	91		82
e	$Br(CH_2)_6Br$	85	$Br(CH_2)_6$	81
f	$PhCH_2Br$	86	$PhCH_2$	15[b)]
g	$Br(CH_2)_3Br$	96[c)]	$(CH_2)_3$	77[d)]
h	$Br(CH_2)_6Br$	87[c)]	$(CH_2)_6$	91[d)]

a) One pot synthesis.

b) The low yield is due to the simultaneous formation of benzoic acid in 60% yield.

c) 

$PhCH(CN)(CH_2)_nCH(CN)Ph$

d) 

$Ph-C(=O)-(CH_2)_n-C(=O)-Ph$

Monoalkylation followed by oxidative decyanation could be also achieved in one pot (example 3a). Oxidative decyanation of δ-halonitriles (2c and 2d) gave cyclopropyl ketones (3c and 3d) instead of γ-haloketones. This seems to be the good method for cyclopropyl phenyl ketone synthesis. It is noteworthy that all synthetic conversions from the starting material to the final product proceed in aqueous medium at room temperature. The combination of cyano and phenyl groups presumably serves for effecting suitable stability and reactivity of the carbanion derived from 2, towards direct oxygenation in aqueous medium. In contrast with the report by Watt, the present oxidative decyanation directly proceeds without any reducing agents. This fact is suggestive of β-elimination reaction that may produce cyanate anion ($^-O-C{\equiv}N$) as a leaving group.

Further studies of the application of direct oxygenation in aqueous medium are in progress.

References and Notes

1) S. J. Selikson and D. S. Watt, J. Org. Chem., 40, 267 (1975) and references cited therein.

2) E. V. Dehmlow, Angew. Chem. Internat. Edit. Engl., 13, 170 (1974); M. Makosza, Pure Appl. Chem., 43, 439 (1975).

3) Y. Masuyama, Y. Ueno, and M. Okawara, Tetrahedron Lett., 1976, 2967.

4) The yields given are for isolated products. All new compounds obtained here exhibited satisfactory spectral and physical properties. Ketones were identified by comparison of their physical properties with those of the authentic samples. The aldol condensation was not observed. Treatment of 1 with allyl bromide and cinnamyl chloride similarly gave the corresponding monosubstituted products (2) in 92% and 93% yields, respectively. Direct oxygenation of these compounds, however, did not afford expected products.

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