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THE REACTION OF O-BENZOYL AROMATIC ALDEHYDE CYANOHYDRIN WITH ALIPHATIC ALDEHYDE

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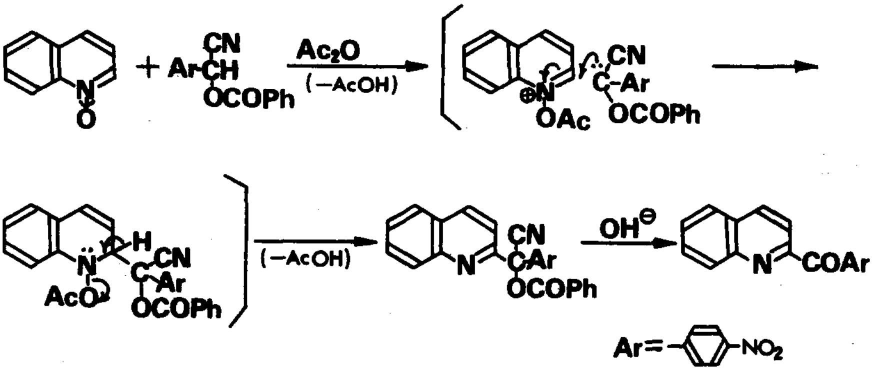
Nucleophilic reaction of aldehyde cyanohydrin derivatives has become of much interest in recent years[1-4]. The preceding paper from our laboratory has described α-aroylation of N-heteroaromatics which involves the reaction of aromatic N-oxides with O-benzoyl aromatic aldehyde cyanohydrins in the presence of acetic anhydride and alkaline hydrolysis of the substituted products thus formed[5]. For example, quinoline N-oxide readily reacts with O-benzoyl p-nitrobenzaldehyde cyanohydrin when heated in acetic anhydride to give O-benzoylcyanohydrin of 2-quinolyl p-nitrophenyl ketone which is easily convertible to the corresponding ketone by heating with 10% sodium hydroxide in methanol as shown below.



We now wish to report a new synthetic method for α-benzoyloxyalkyl aryl ketones by the reaction of O-benzoyl aromatic aldehyde cyanohydrins[6] with aliphatic aldehydes in the presence of potassium carbonate in tert-butanol.

A mixture of O-benzoyl mandelonitrile (I: Ar=Ph) (6g, 0.025 mole), acetaldehyde (2.2g, 0.05 mole) and potassium carbonate (7g, 0.05 mole) in tert-butanol (30 ml) was stirred at room temperature for 6 hours, and insoluble substances were filtered. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography on alumina with dichloromethane-n-hexane (1:1) and recrystallized from ethanol to give O-benzoate of 2-hydroxypropiophenone (III: Ar=Ph, R=CH_3), colorless plates, mp 107-109° (lit.[1] 108-109°), in 59.4% yield.

Structure assignment of the product is based on the satisfactory elemental analysis [$C_{16}H_{14}O_3$], the IR spectrum [ν_{max}^{Nujol}: 1690 and 1720 cm^{-1}] and the NMR spectrum [τ ($CDCl_3$) : 8.30 (3H, d, J=7 Hz, $\underline{H_3}C$-CH<), 3.80 (1H, q, J=7 Hz, CH_3-C$\underline{H}$<), 2.50 (6H, m, meta and para aromatic protons), 1.95 (4H, m, ortho aromatic protons)].

Similar reactions were carried out under the same conditions using various O-benzoyl aromatic aldehyde cyanohydrins and aliphatic aldehydes, and the results shown in Table were obtained. Among conditions so far examined, the above-mentioned one was found to be most effective for the proceeding of the reaction, the use of stronger bases such as ethanolic sodium ethoxide giving no satisfactory results.

Kuebrich and Schowen[1] have described that the reaction of benzil with cyanide ion gives the carbanion II (Ar=Ph) which behaves as "active aldehyde" and attacks at electrophiles present in the reaction systems. Thus they obtained III (Ar=Ph, R=CH_3) in unreported yield from the reaction in the presence of acetaldehyde. The present reaction is apparently initiated by the formation of the carbanion II and follows the same course with that advanced by Kuebrich and Schowen[1].

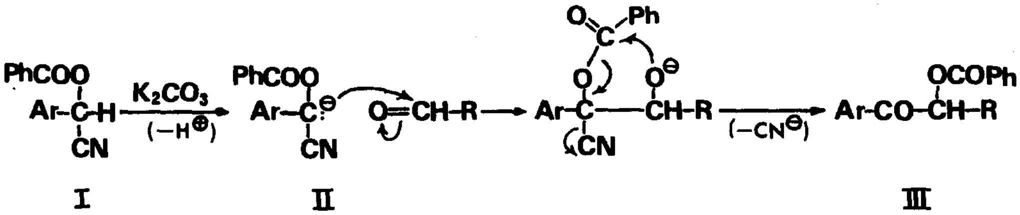


Table Reactions of O-benzoyl aromatic aldehyde cyanohydrins with aliphatic aldehydes

Ar	R	Yield of III (%)[a)]	mp(°C) or bp(°C/mmHg)
Ph	CH_3	59.4	107-109
Ph	CH_3CH_2	46.3	155-163/0.35
Ph	$(CH_3)_2CH$	37.0	162-164/0.4
p-NO_2-C_6H_4	CH_3	74.2	121-122
p-CN-C_6H_4	CH_3	52.4	115-116
p-MeO-C_6H_4	CH_3	14.2	106.5-107.5
p-Cl-C_6H_4	CH_3	17.7	83-84
2-pyridyl	CH_3	71.6	154-156/0.3

a) Based on O-benzoyl aldehyde cyanohydrins (I).

The scope of this reaction of Benzoin condensation type seems to be fairly widespread and the procedure described here is more convenient and advantageous for the synthetic purpose than that starting from benzil[1]. Further examinations on transformation of products III and also on extension of this type of reaction are underway in our laboratory.

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