

Cyanoethylation of methyl and ethyl ethers of dimethylphenols

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ABSTRACT

The C-cyanoethylation of the methyl and ethyl ethers of dimethylphenols has been carried out with acrylonitrile in the presence of anhydrous AlCl_3 to furnish propionitrile derivatives. The latter on hydrolysis to the corresponding propionic acids followed by cyclization with PPA afforded the appropriate indanones, whose structures have been established on the basis of spectral data and by the formation of 2, 4-DNP derivatives.

1. INTRODUCTION

IN continuation of our earlier work¹ on the cyanoethylation of some methyl and ethyl ethers of phenols² leading to the synthesis of polycyclic compounds we describe here the synthesis of indanones obtained from some methyl and ethyl ethers of dimethylphenols by the application of cyanoethylation.

The cyanoethylation was carried out using five moles of acrylonitrile per mole of the phenol ether in the presence of anhydrous AlCl_3 and tetrachloroethane as a solvent. Dry HCl gas was passed through the reaction mixture kept at $0-10^\circ$ for 1.5 hr and later and $95-100^\circ$ for another 1.5 hr. The yields of the resultant nitriles varied with the nature of the phenolic compounds and ranged from 15-30%. Passing dry HCl gas for longer periods did not improve the yields. Out of the different catalysts used in the reaction, anhydrous AlCl_3 (1 mole) was found to be the most suitable. Also, amongst the various solvents such as ether, THF, etc., tried for the reaction, sym-tetrachloroethane (4 moles) was found to be the most convenient,³ especially when working with small amounts of the alkoxy compounds. It gave better yields of the nitriles and purer products. These nitriles (mono- or di-) analysed correctly and were hydrolysed by boiling with conc. HCl for 3 hr to give the corresponding (mono- or di-) carboxylic acids, as solids.

The mono-carboxylic acids underwent PPA-cyclization smoothly to the corresponding indanone derivatives, whose structures were supported by their analytical and spectral data. The indanones readily formed crystalline 2, 4-DNP derivatives and were reduced with LAH to indanols. Indanone (II) was converted to the corresponding indene (b.p. 155–160°/2–2.5 mm) by heating the appropriate indanol (m.p. 105–106°) with oxalic acid. The structures of the indanones were confirmed by their nmr spectral data wherever required.

It has been observed from our previous¹ and the present work that in nuclear cyanoethylation the position para to the alkoxy group is preferentially attacked when ortho and para positions are free. Cyanoethylation occurs in ortho position only when the para position is blocked. It was also found that di-cyanoethylation occurred readily when both the ortho positions and para positions were available and no monocyanoethylated products were obtained. Similarly, all attempts to prepare tricyanoethylated compounds from these ethers were futile.

In the case of ethers of 2, 3-dimethyl and 2, 5-dimethylphenols, the ortho position being blocked, the cyanoethylation occurred at the para position giving a monocyanoethylated product. Here again attempts to obtain dicyanoethylated product were unsuccessful.

In the case of the ethers of 2, 6-dimethylphenol, the reaction took place at the position para- to the alkoxy group. It was interesting to note that during hydrolysis of the nitrile *Ia* with conc. HCl demethylation also occurred. This was confirmed as follows: Hydrolysis of the *Ia* with hydrogen bromide in acetic acid yielded the propionic acid *Ib*. When *Ib* was boiled with methyl iodide in the presence of anhydrous potassium carbonate, an ester was obtained which on hydrolysis with dil. HCl afforded the methyl ether of *Ib*. All attempts to cyclize the acid (*Ib*) to an indanone derivative, met with failure.

In the case of ethers of 2, 4-dimethyl- and 3, 4-dimethylphenols, the 4-(para) position being blocked the cyanoethylation occurred at the 6-(ortho) position to give a monocyanoethylated product. Here also, attempts to obtain dicyanoethylated products were unsuccessful. In the case of ethers of 3, 5-dimethylphenol as stated above, since both the ortho positions and also the para position are accessible, the cyanoethylation afforded a dicyanoethylated product.

The results with the methyl and ethyl ethers of dimethylphenols were identical in all cases. The percentage yields of the cyanoethylated products were almost the same in both the cases.

Table 1. Physical data of various compounds prepared.

Ether†	Propionitrile*	Propionic acid*	Indanone* (yield)
1. 2, 6-Dimethyl-1-methoxybenzene. ⁴	(I a): 4-Mono-, yellow needles**, m.p. 133–135°.	(I b): Colourless needles***, m.p. 114–116°.	..
2. 3, 4-Dimethyl-1-methoxybenzene. ⁵	6-Mono-; colourless oil, b.p. 162–164°/3–5 mm.	6-Mono-; colourless needles****, m.p. 88–90°.	(II): yellow needles****, m.p. 122–124° (70%), 2, 4-DNP, red needles, m.p. > 310°.
3. 3, 5-Dimethyl-1-methoxybenzene. ⁴	(III a): 2, 4-Di-, colourless needles****, m.p. 95–96°.	(III b): 2, 4-Di-, colourless needles****, m.p. 149–151°.	..
4. 2, 3-Dimethyl-1-ethoxybenzene. ⁶	4-Mono-; yellow needles*****, m.p. 75–77°.	4-Mono-; colourless needles**, m.p. 114–116°.	(IV): Yellow needles**, m.p. 105–106° (70%), 2, 4-DNP, red prisms, m.p. 240–242°.
5. 2, 4-Dimethyl-1-ethoxybenzene. ⁶	6-Mono-; colourless oil, b.p. 165–166°/2–2.5 mm.	6-Mono-; colourless oil, b.p. 160–161°/1–1.5 mm.	(V): Brownish-red oil (40%). 2, 4-DNP; red needles, m.p. > 320°.
6. 2, 5-Dimethyl-1-ethoxybenzene. ⁷	4-Mono-; white needles**, m.p. 49–51°.	4-Mono-; white needles**, m.p. 114–116°.	(VI): Yellow needles**, m.p. 153–155° (45%), 2, 4-DNP, red needles, m.p. 259–260°.
7. 2, 6-Dimethyl-1-ethoxybenzene. ⁴	(VII): 4-Mono-; colourless needles**, m.p. 130–133°.	(I b): 4-Mono-; colourless needles**, m.p. 114–116°.	..
8. 3, 4-Dimethyl-1-ethoxybenzene. ⁶	6-Mono-; colourless oil, b.p. 188–190°/2 mm.	6-Mono-; colourless needles**, m.p. 100–102°.	(VIII): Pink needles**, m.p. 113–115° (72%), 2, 4-DNP as red prisms, m.p. > 300°.
9. 3, 5-Dimethyl-1-ethoxybenzene. ⁴	(IX a): 2, 4-Di-; colourless needles**, m.p. 83–85°.	(IX b): 2, 4-Di-; colourless needles**, m.p. 147–149°.	..

* All compounds gave satisfactory elemental analysis.

** Crystallized from benzene-petroleum ether (40–60°).

*** Crystallized from ethyl acetate.

**** Crystallized from ethyl acetate-petroleum ether (40–60°).

***** Crystallized from petroleum ether (40–60°).

† Numbers given in superscript in this column relate to references.

(II): UV $\lambda_{\text{max}}^{\text{MeOH}}$ 260 (log ϵ 3.94), 325 (log ϵ 3.57) nm. IR: (Nujol): 1692 (CO), 1600, 1494, 900 (aromatic) cm^{-1} ; NMR: (δ , CHCl_3): 2.3 (3H, s, $\text{CH}_3(a)$), 2.5 (3H, s, $\text{CH}_3(b)$), 2.7 (2H, t $\text{CH}_2(c)$), 2.8 (2H, t, $\text{CH}_2(d)$), 3.85 (3H, s, OCH_3), 6.8 (1H, s, $\text{H}_{(e)}$).

(III b): NMR (δ , CDCl_3): 2.3 (6H, s, 2CH_3), 2.58 (4H, m, $-2\text{CH}_2 \beta$ to $-\text{COOH}$), 3.00 (4H, m, $-\text{CH}_2 \alpha$ to $-\text{COOH}$), 3.80 (3H, s, $-\text{OCH}_3$), 6.58 (1H, s, aromatic proton), 11.28 (2H, s, -2COOH).

2. GENERAL PROCEDURE FOR NUCLEAR CYANOETHYLATION

Finely powdered anhydrous aluminium chloride (5.3 g) was added slowly to a vigorously stirred cold solution of ether of a dimethylphenol (0.005 mole) and acrylonitrile (13.3 ml) in a dry system containing tetrachloroethane (40 ml). Dry hydrogen chloride was passed through the reaction mixture maintained at 10–15° for 1.5 hr. The reaction mixture was then heated on a water bath maintained at 90–95° for 1.5 hr with the continuous passage of dry hydrogen chloride. The dark red material was decomposed with ice and extracted with ether. The ether layer was washed with water and dried. Removal of ether left behind a pinkish-red liquid, which was distilled under vacuum. Tetrachloroethane distilled over first and the residual mass distilled later at higher temperature. On cooling it often solidified and crystallized from appropriate solvents in good crystals.

3. HYDROLYSIS OF THE PROPIONITRILES

The above nitriles (1.2 g) were refluxed with concentrated hydrochloric acid (120 ml) for 3 hr. The solution was then cooled and extracted with chloroform. On removal of the chloroform a solid separated which was dissolved in sodium bicarbonate solution. It was again extracted with chloroform and the bicarbonate layer was acidified with conc. HCl. It was again extracted with chloroform, washed with water and dried over anhydrous sodium sulphate. Removal of the solvent left behind a solid, crystallized from suitable solvents.

4. CYCLISATION OF THE PROPIONIC ACIDS

The acids (300 mg) were added to a mixture of phosphorus pentoxide (10 g) and phosphoric acid (4 ml) preheated at 100° for 0.5 hr and heating was continued for a further 2 hr with occasional shaking. The mixture was cooled, decomposed with water and extracted with chloroform. The solvent layer was washed well with sodium bicarbonate solution, water and dried. Removal of the solvent yielded a solid, crystallized from appropriate solvents.

The 2, 4-DNPs of the above indanones were crystallized from acetic acid.

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