A New Simple Catalyst for the Synthesis of 1,3-Diols and Their Monoesters from Linear Aliphatic Aldehydes

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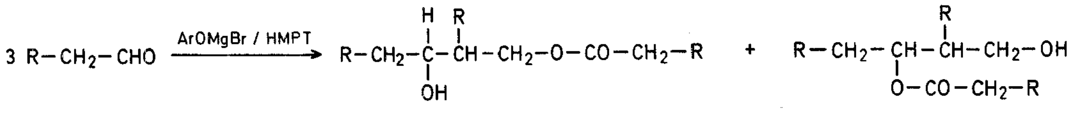
Glycol monoesters have been previously obtained in "one step" syntheses from linear aliphatic aldehydes using simple[1,2,3,4] or complex[3,4] magnesium, boron, and aluminum alkoxides. The yields are usually very low with the former and higher with the latter, although in this case the preparation of the catalyst is more complex.

Recently, we have found that, by using magnesium salts of phenols as metalating agents for linear aliphatic aldehydes, selective autocondensation processes occurred and were dependent on the solvent and the ion pair used[5]. In particular, when aliphatic aldehydes reacted with 2,4,6-trimethylphenoxymagnesium bromide with a ratio 1 : 1 in hexamethylphosphoric triamide, a mixture of 1,3-diol monoesters **1** and **2** was produced in high yield.

This finding appeared rather promising from a synthetic point of view; therefore we further explored the reaction



$$3\ R{-}CH_2{-}CHO \xrightarrow{ArOMgBr\ /\ HMPT} R{-}CH_2{-}\underset{OH}{\overset{H}{C}}{-}\overset{R}{CH}{-}CH_2{-}O{-}CO{-}CH_2{-}R \quad + \quad R{-}CH_2{-}\underset{O-CO-CH_2-R}{CH}{-}\overset{R}{CH}{-}CH_2{-}OH$$

R = *n*-alkyl

1 **2**

Table 1. Synthesis of 1,3-Diol Monoesters from Linear Aliphatic Aldehydes[a]

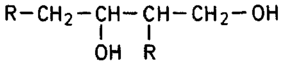
	R	Time (h)	Conversion (%)	Yield of **1**+**2**[b,c] (%)	b.p.	b.p. (lit.[3])
a	CH_3	2	95	72	70–71°/1 torr	92–94°/2 torr
b	C_2H_5	3	100	72	71–72°/0.03 torr	103–104°/0.5 torr
c	C_3H_7	2	100	92	128–129°/1.2 torr	138–139°/1 torr
d	C_4H_9	2	100	91	115–116°/0.15 torr	150–152°/1 torr
e	C_5H_{11}	5	82	73	139–140°/0.01 torr	167–170°/0.5 torr
f	C_8H_{17}	2	100	75	177–180°/0.001 torr	—

[a] T = 40°; ratio aldehyde/C_6H_5OMgBr = 10.

[b] By G.L.C.

[c] Difference to 100 is represented mainly by the correspondent glycols and their diesters.

Table 2. Synthesis of the corresponding 1,3-diols (3)


$R-CH_2-CH(OH)-CH(R)-CH_2-OH$

3

R	Yield (%)[a]	b.p.	b.p. (Lit. value)
CH_3	50	86–87/1 torr	85–86/1 torr
C_2H_5	57	110–111/1 torr	94–96/0.5 torr
C_3H_7	52	94–95/0.2 torr	107–108/1 torr
C_4H_9	53	128–129/0.5 torr	128–129/1 torr
C_5H_{11}	49	128–130/0.2 torr	125–127/0.5 torr
C_8H_{17}	50	200–203/0.1 torr	—

[a] Yields refer to the isolated products and are based on the starting aldehyde.

conditions and the influence of several catalysts in order to achieve good yields using cheaper phenols and a higher aldehyde: catalyst ratio.

We report now the results obtained using unsubstituted phenoxymagnesium bromide in catalytic amounts in hexamethylphosphoric triamide (see Table 1). In this case the electrophilic attack by the carbonyl group of the aldehyde on the aromatic nucleus of the phenoxymagnesium bromide, which easily occurred in benzene[6], forcing us to use 2,6-substituted phenols as catalysts, is completely depressed. Conversion and yields are in all cases higher than those reported in literature. We were not able to separate products **1** and **2** by vacuum distillation or by G.L.C. on low polarity columns on which the analysis reported in Table 1 were performed. Nevertheless, by N.M.R. and G.L.C. analysis on polar columns (dinonyl phthalate 5%, neopentylglycol succinate 5%) it was possible to determine that **1** is in all cases the main component of the isolated (**1**+**2**) mixture (**1**:**2**= 1·5 to 2·0)[7].

Hydrolysis of the crude reaction product with alcoholic potassium hydroxide gave the corresponding 1,3-diols (**3**) in good yields (Table 2). Alternative routes for 1,3 diols (**3**) could be the reduction of the correspondent aldols, which however, are very difficult to prepare in good yields, especially from *n*-alkanals of more than six carbon atoms[8]. This consideration, together with the very simple procedure necessary to obtain 1,3-diols from the aldehydes, allows us to overcome the less favourable stoichiometry (2/3 of the starting aldehyde are converted into 1,3-diols) which lowers the overall yield of the reactions.

Synthesis of 1,3-Diol Monoesters:

The procedure was carried out under a stream of nitrogen. Magnesium turnings (0.05 g-atom) were suspended in anhydrous diethyl ether (50 ml) and a slight excess of ethyl bromide in ether was slowly added to allow a gentle reflux. When the magnesium was completely dissolved, phenol (0.05 mol) in diethyl ether was added dropwise.

The ether was then distilled off and gradually replaced by hexamethylphosphoric triamide (150 ml). Removal of the ether was finally achieved by heating the solution at 90° for 30 min. After cooling, a hexamethylphosphoric triamide solution (~100 ml) of the aldehyde (0.5 mol) was added dropwise and the mixture was allowed to stand at 40° for the time required to give a good conversion (see Table 1). The reaction mixture was then treated with a saturated ammonium chloride solution and extracted with ether; the combined ethereal extracts were transferred into a separatory funnel and washed with a 1 *N* solution of potassium hydroxide (~200 ml) in order to remove the phenol, then with water, and were finally dried over sodium sulfate. The 1,3-diols monoesters were isolated as a mixture of **1** and **2** by vacuum distillation.

For quantitative G.L.C. analyses, suitable internal standards and the following columns (150 cm × 1/8 inch stainless steel; silanized Chromosorb W 60/80 as solid support) and conditions were used: SE 30 5% T=100° for **1a**+**2a**; T=120° for **1b**+**2b**; T=225° for **1e**+**2e**; T=250° for **1f**+**2f**; DEGS 10% T=165° for **1c**+**2c**; XE 60 3% T=185° for **1d**+**2d**.

Synthesis of 1,3-Diols:

The crude product, obtained by the procedure previously described, was treated with a solution of potassium hydroxide (20 g) in ethanol (150 ml) under reflux for 3 h. To the residue left by removal of most solvent by distillation, water (100 ml) was subsequently added and the mixture extracted 7–8 times with ether (~50 ml). The ethereal extracts, dried over sodium sulfate, on evaporation gave a crude product (90–95% purity by G.L.C.). The pure 1,3-diols were obtained by vacuum distillation.

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