REDUCTION OF 4-HYDROXY-3,5-DIALKYLBENZALDEHYDES WITH COMPLEX HYDRIDES OF ALKALI METALS

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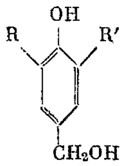
The reduction of carbonyl compounds in the series of sterically hindered phenols can be a convenient method for the preparation of various phenols of a similar type. Thus, when 4-hydroxy-3,5-di-tert-butylacetophenone is treated with aluminum lithium hydride, even under mild conditions, complete hydrogenolysis of the carbonyl group occurs with the formation of 4-ethyl-2,6-di-tert-butylphenol [1]. It was interesting to study this reduction reaction on the example of various 4-hydroxy-3,5-dialkylbenzaldehydes.

Alkyl substituents, differing in character, should affect the basicity of the oxygen of the carbonyl group to different degrees, since the interaction of the p-electrons of the phenolic oxygen with the π-electrons of the benzene ring increases with increase in the steric shielding of the phenolic hydroxyl [2]. In view of this a difference could also be expected in the behavior of 4-hydroxy-3,5-dialkylbenzaldehydes during their reduction. A communication exists in the literature, without giving any indications of the reaction conditions, on the reduction of 4-hydroxy-3,5-di-tert-butylbenzaldehyde with aluminum lithium hydride, leading to the formation of 4-hydroxy-3,5-di-tert-butylbenzyl alcohols [3]. According to our data, 4-methyl-2,6-di-tert-butylphenol is formed and about 50% of the 4-hydroxy-3,5-di-tert-butylbenzaldehyde fails to react when 4-hydroxy-3,5-di-tert-butylbenzaldehyde is reduced with an equimolar amount of aluminum lithium hydride. The 4-methyl-2,6-di-tert-butylphenol is formed in 85% yield when a three-fold excess of the reagent is used, in which connection the presence of 4-hydroxy-3,5-di-tert-butylbenzyl

TABLE 1. 4-Hydroxy-3,5-dialkylbenzyl Alcohols



R	R′	Mp, °C (solvent)	R_f (benzene — methanol, 9:1)	Yield, %	Empirical formula	Found, % C	Found, % H	Calculated, % C	Calculated, % H
CH_3	CH_3	104—105* (benzene)	0,18	78					
$CH(CH_3)_2$	$CH(CH_3)_2$	62—63 (hexane — CCl_4)	0,29	77	$C_{13}H_{20}O_2$	75,19 75,24	9,75 9,84	75,01	9,61
CH_3	$C(CH_3)_3$	90—92 (hexane — CCl_4)	0,28	89	$C_{12}H_{18}O_2$	73,95 73,12	9,58 9,62	74,16	9,38
CH_3	C_6H_{11}	102—103 (hexane — CCl_4)	0,23	77	$C_{14}H_{20}O_2$	75,86 76,12	9,03 9,22	76,36	9,09
CH_3	Bornyl	129—130 (hexane — CCl_4)	0,27	91	$C_{18}H_{27}O_2$	78,51 78,72	9,36 9,41	78,83	9,88
C_6H_{11}	C_6H_{11}	136—137 (hexane)	0,36	94	$C_{19}H_{28}O_2$	79,39 79,41	9,81 9,64	79,29	9,72
$C(CH_3)_3$	$C(CH_3)_3$	139—140 †	0,45	74					

* From [5]: mp 104.5-105°.

† From [6]: mp 137-138°.

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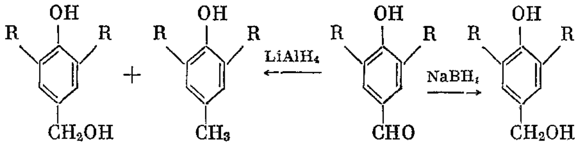
TABLE 2. Reaction Products of 4-Hydroxy-3,5-dialkylbenzaldehydes and Aluminum Lithium Hydride

R*	R†	4-Hydroxy-3,5-dialkylbenzyl alcohols			2,4,6-Trialkylphenols	
		yield, %	Mp, °C	R_f (benzene–methanol, 9 : 1)	yield, %	R_f (benzene – methanol, 9:1)
CH_3	CH_3	92	104-106	0.18	-	
$CH(CH_3)_2$	$CH(CH_3)_2$	56	62-63	0.29	33	0.71
CH_3	$C(CH_3)_3$	44	90-92	0.28	37	0.74
C_6H_{11}	C_6H_{11}	66	136-137	0.37	28	0.82
$C(CH_3)_3$	$C(CH_3)_3$	1	-	0.45	85	0.91

* Substituent in the 3 position.

† Substituent in the 5 position.

alcohol can be detected only chromatographically. The 2,4,6-trialkylphenols and corresponding 4-hydroxy-3,5-dialkylbenzyl alcohols were now obtained in commensurate amounts when this reaction was run with the 4-hydroxy-3,5-diisopropyl- and 4-hydroxy-3-methyl-5-tert-butylbenzaldehydes. Even in the presence of excess aluminum lithium hydride, the reduction of 4-hydroxy-3,5-dimethylbenzaldehyde results in the formation of the hydroxyarylbenzyl alcohol. More unambiguous results are obtained when the 4-hydroxy-3,5-dialkylbenzaldehydes are reduced with sodium borohydride in methyl alcohol. The hydrogenolysis of the carbonyl group no longer occurs with this reducing agent, but in excess reducing agent the methyl ester of the corresponding hydroxyalkylbenzyl alcohol is formed in certain cases. The main reaction product is always the indicated alcohol



The optimum yields (75-95%) of the 4-hydroxy-3,5-dialkylbenzyl alcohols are achieved when a 2- to 4-fold excess of sodium borohydride is used. These results are found to be in agreement with the data that were obtained in the reduction of certain 4-hydroxy-3,5-di-tert-butyl alkyl ketones with aluminum lithium hydride and sodium borohydride [1, 4].

The separation of the reaction products was effected chromatographically on a thin layer of aluminum oxide, in the solvent system: benzene–methanol (9 : 1). The 2,4-trialkylphenols were also identified by GLC.

EXPERIMENTAL METHOD

Reduction of 4-Hydroxy-3,5-dialkylbenzaldehydes with Sodium Borohydride. To a solution of 0.05 mole of the 4-hydroxy-3,5-dialkylbenzaldehyde in 50 ml of methyl alcohol was added 0.15-0.2 mole of sodium borohydride in 10 ml of water. After 2 h the reaction mixture was treated with 10% HCl solution and then water. The obtained oil was extracted with ether, dried over $MgSO_4$, the solvent was vacuum-distilled, and the residue was recrystallized. The physical constants and yields of the obtained compounds and the elemental analysis data are given in Table 1.

Reduction of 4-Hydroxy-3,5-dialkylbenzaldehydes with Aluminum Lithium Hydride. To 0.03 mole of $LiAlH_4$ in 50 ml of ether was added 0.01 mole of the 4-hydroxy-3,5-dialkylbenzaldehyde in 50 ml of ether. The reaction mixture was refluxed for 3 h, allowed to stand for a day at 20°C, and then it was treated with 10% H_2SO_4 solution. The organic layer was dried over $MgSO_4$, the solvent was vacuum-distilled, and the residue was chromatographed as a thin layer on aluminum oxide (benzene–methanol, 9 : 1) (see Table 2). The fraction with R_f 0.18-0.5 was recrystallized from hexane. The fraction with R_f 0.6-0.9 was vacuum-distilled and then analyzed by GLC (Tswett chromatograph equipped with a flame-ionization detector, and using 15% poly(ethylene glycol adipate) deposited on Celite C22 as the stationary phase).

CONCLUSIONS

A study was made of the reduction of seven 4-hydroxy-3,5-dialkylbenzaldehydes with aluminum lithium hydride and sodium borohydride.

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