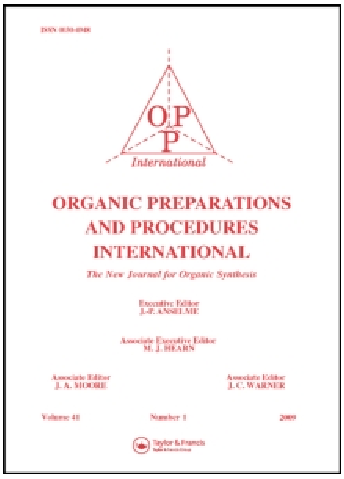

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HALOGEN AS A READILY CLEAVABLE PROTECTIVE GROUP FOR REACTIVE POSITIONS IN PHENOLS AND PHENOLIC COMPOUNDS

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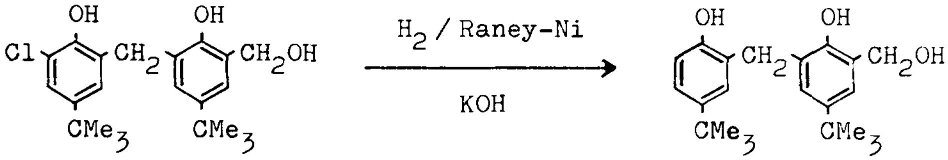
Some recent publications described different protective groups for reactive positions in phenols[1a,c,f] and phenolic compounds like dihydroxydiphenyls[1b] and dihydroxydiphenylmethanes.[1d,e,g] For instance, *t*-butyl groups[1a,b,d] or bromine atoms[1c] could be eliminated by the treatment with $AlCl_3$ in benzene or toluene at 20 - 50°. For the elimination of bromine or chlorine atoms, the reaction with nickel-aluminium alloy in 10% aqueous sodium hydroxide at 95 - 97° was proposed as an alternative.[1e,g] In this context, it seems useful to recall[2] that halogen atoms can be eliminated in a similar manner which however, requires only very mild reaction conditions.

The phenolic compound is dissolved with cooling in a solution of sodium or potassium hydroxide in methanol, Raney-Ni is added, and the mixture is treated at room temperature un-



der atmospheric pressure with hydrogen in a simple apparatus with shaking or stirring. Although a 10% excess of the base generally is used with respect to the halogen atoms, in some cases a larger excess can be utilized to improve the solubility of the phenolic compound. For oligonuclear phenolic compounds with higher molecular weights, better solubility can also be achieved by the addition up to 50% of dioxane. On the other hand, with readily soluble phenolic derivatives, the addition of water may be advantageous in order to keep the sodium or potassium halogenide which is formed, in solution. In some cases, the reaction may be carried out entirely in aqueous solution. The dehalogenation can be easily and quantitatively followed by the hydrogen uptake which is usually complete within a few hours. The elimination of chlorine atoms sometimes requires slightly elevated temperatures (50°); however this also depends on the activity of the Raney-Ni. Thus for the preparation of very sensitive compounds, the use of bromine atoms as protective groups may be preferable, although during condensation reactions chlorine may be more stable.[3] When the hydrogenation is completed, the catalyst is filtered and the alkaline filtrate is dripped into diluted aqueous acid with cooling. The reaction product which precipitates is normally chromatographically pure, when pure starting compounds are used.

By the procedure outlined above, many different oligonuclear phenolic compounds have been prepared.[4] This method cannot be used if substituents are present which will be also reduced under the reaction conditions. On the other hand, a selective reduction of those groups (e.g. aldehyde functions) can be achieved in neutral or acid solution without any attack on the halogen atoms. In contrast to the previously mentioned methods,[1] the reaction conditions of the dehalogenation are so mild that also very sensitive compounds like phenolic alcohols can be prepared. The following general experimental procedure involves such a compound which most probably can neither be obtained in strongly alkaline solutions at high temperatures nor in the presence of a strong Lewis acid like $AlCl_3$, at least not in pure form. In the same way, many similar compounds, containing up to seven phenolic units, could be synthesized.[5]

EXPERIMENTAL

3-(5-t-Butyl-2-hydroxy-benzyl)-5-t-butyl-2-hydroxy-benzyl alcohol.- To a solution of 3.77 g. (0.01 mole) of 3-(5-*t*-butyl-3-chloro-2-hydroxy-benzyl)-5-*t*-butyl-2-hydroxy-benzyl alcohol[6] in a mixture of about 30 ml. of methanol and 10 ml. of dioxane, was added a cooled solution of 0.62 g. (0.011 mole) of KOH in 5 ml. water and about half a tea spoon of wet Raney-Ni.[7] The hydrogenation was carried out at room temperature under atmospheric pressure. When the hydrogen uptake was complete, the catalyst was removed by suction and the filtrate was slowly dripped into dilute (about 0.5 - 1%), ice-cold, aqueous HCl. The white precipitate was filtered by suction and carefully washed with water to remove all traces of acid. By recrystallization from toluene/petroleum ether (70 - 100°), 78% of chromatographically pure, white crystals were obtained, mp. 155°.

Anal. Calcd. for $C_{22}H_{30}O_3$ C, 77.15 H, 8.83 mol. weight 342.5

Found C, 77.34 H, 8.87 mol. weight 345[8]

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7. Several different samples of Raney-Ni (Degussa) were used in these preparations and commercially available Raney-Ni (e.g. Merck-Schuchardt) may be used with the same success.
8. Determined by vapor pressure osmometry in benzene.

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