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REDUCTIONS WITH NICKEL-ALUMINUM ALLOY AND AQUEOUS ALKALI

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PART I. THE CARBONYL GROUP

Since the report by Whitman, Wintersteiner, and Schwenk (1) on the reduction of estrone to a mixture of alpha- and beta-estradiol by a nickel-aluminum (Raney) alloy in alkaline solution there has appeared in the literature, as far as we could determine, but one instance (2) of the use of this reduction method. During the course of other investigations, we have had the opportunity to study further the reducing action of this alloy. This first paper represents the results we have obtained with compounds containing the carbonyl group.

Compounds of this type usually take up hydrogen quite easily when treated with nascent hydrogen, or with hydrogen in the presence of a catalyst, to give the corresponding alcohols. Occasionally, even reduction to the hydrocarbon has been observed. A more general method of obtaining the hydrocarbon is by the Clemmensen reduction, which, however, has not always given satisfactory results (3, 4). Alternative methods for accomplishing the transformation of carbonyl compounds to the hydrocarbons are the Wolff-Kishner reduction and catalytic hydrogenation.

We have found that with many carbonyl compounds our reduction method gives results comparable to those obtainable by the Clemmensen reduction. However, unlike the Clemmensen reduction, our reduction method is not specific, in that it converts carbonyl compounds to either the corresponding carbinol or the hydrocarbon, the extent of the reduction depending solely on the structure of the carbonyl compound. Carbonyl compounds of the general formula I

$C_6H_5C=OR$	$C_6H_5(CH_2)_xC=OR'$
Ι	II
R = H, alkyl or aryl;	$\mathbf{R}' = \mathbf{H}$ or alkyl

yield the hydrocarbon, whereas carbonyl compounds of the general formula II yield the carbinol.

It is apparently necessary that the carbonyl group be directly attached to an aromatic carbon atom, formula I, forming a conjugated system, in order to obtain reduction of the carbonyl group to the hydrocarbon. However, when the carbonyl group, even as part of a conjugated system, is not directly attached to an aromatic carbon atom, formula II, the reduction of the carbonyl group proceeds only as far as the alcohol. Thus, while benzaldehyde gives toluene, and acetophenone gives ethylbenzene, cinnamic aldehyde and salicylacetone are only reduced to hydrocinnamyl alcohol and 4-(o-hydroxyphenyl)butanol-2, respectively.

As in the Clemmensen reduction, benzyl alcohol and *p*-hydroxybenzyl alcohol

are reduced to toluene and *p*-cresol, respectively. Other functional groups in addition to the carbonyl group, such as the nitro group, which is reduced to the amine, may be reduced as usual without interfering with the reduction of the carbonyl group.

With compounds soluble in alkali, the reduction proceeds smoothly to the desired product in good yield (70–90%). Difficulties are encountered with most of the carbonyl compounds which are insoluble in alkali. They are either not reduced or yield intermediate reduction products. However, we have found that the reduction of a great majority of these insoluble compounds proceeds satisfactorily to the hydrocarbon or the alcohol in the presence of a suitable solvent such as alcohol and/or toluene. For example, benzil without solvent gives a mixture of intermediate reduction products, whereas with alcohol as solvent dibenzyl was obtained exclusively.

We have also encountered several interesting examples of alkali-insoluble compounds which yield different reduction products with different solvents. Anisil, which was not reduced without solvent, gave in the presence of toluene anisoin as the only reduction product, and with toluene and alcohol as solvent hydroanisoin was obtained. However, in none of these experiments did we obtain any 4,4'-dimethoxydibenzyl. Dibenzalacetone also proved an interesting example of the effect of solubility on the course of the reduction. With no solvent or with alcohol as solvent, dibenzalacetone was recovered unchanged. With toluene as solvent, the only product obtained, besides some unchanged dibenzalacetone, was 1,5,6,10-tetraphenyl-3,8-diketodecadien-2,9 (5). Notwithstanding the fact that this compound contains four potentially reducible groups, attempts to reduce it further were unsuccessful.

The procedure employed for these reductions is essentially that described for the preparation of Raney's nickel hydrogenation catalyst (6). The nickelaluminum alloy is added gradually to an alkaline solution of the carbonyl compound, and the reduction proceeds with the liberation of the hydrogen from the alloy. It appears possible that the reduction is due to the liberation of hydrogen which is then activated by the presence of the nickel catalyst, because we have been able to obtain reduction of the carbonyl group by using aluminum in conjunction with the previously prepared nickel catalyst. In these cases, if the nickel catalyst is omitted and only aluminum used, either no reduction occurs or amorphous products are obtained from which we could not isolate any pure substances. Although we have obtained, with most of the carbonyl compounds which we have studied, identical results in the reductions with either the nickel-aluminum alloy or the aluminum-nickel catalyst combination, we have found that some of the carbonyl compounds, especially those insoluble in alkali, require with the latter reducing agent excessive amounts of aluminum for complete reduction. In Table I are listed the carbonyl compounds and several alcohols which we have reduced by this method.

EXPERIMENTAL

General procedure. The procedure employed is essentially that previously described (1) with the following modifications. Ten grams of the compound is dissolved in 300 ml.

of 10% sodium hydroxide, heated to 90°, and 30 g. of Raney's nickel-aluminum alloy is added in small portions with stirring. The reaction mixture is stirred for an additional hour, the temperature being maintained at 90°. The original volume is maintained by the addition of water. A few drops of octyl alcohol are added occasionally to prevent any excessive foaming. Although this treatment is usually sufficient to complete the reduction

COMPOUND	REDUCTION PRODUCT	XIELD ^a , %
Benzyl alcohol ^b	Toluene	70
o-Hydroxybenzyl alcohol	o-Cresol	85
Benzaldehyde	Toluene	60
Salicylaldehyde ^b	o-Cresol	75
p-Hydroxybenzaldehyde	p-Cresol	80
Cinnamic aldehyde ^c	Hydrocinnamyl alcohol	50
Acetophenone	Ethylbenzene	70
<i>m</i> -Nitroacetophenone ^c	m-Aminoethylbenzene	76
p-Hydroxyacetophenone	p-Ethylphenol	72
p-Hydroxypropiophenone	<i>p</i> -Hydroxypropylbenzene	78
p-Hydroxybenzophenone ^b	<i>p</i> -Hydroxydiphenylmethane	90
2-Methylcyclohexanone ^c	2-Methylcyclohexanol	80
Dibenzyl ketone ^c	Dibenzyl carbinol ^d	70
Salicylacetone ^b	4-(o-Hydroxyphenyl)butanol-2	85
p-Hydroxybenzalacetophenone	<i>p</i> -Hydroxydiphenylpropane ^e	50
Dibenzalacetone ¹	1,5,6,10-Tetraphenyl-3,8-diketo-	
	decadien-2,9°	50
Desoxybehzoin ^c	Dibenzyl ^h	70
Benzoin ^c	Dibenzyl ^h	50
Benzil ^c	$Dibenzyl + desoxybenzoin^i$	
Anisil [†]	Anisoin	80
Anisil ⁱ	Hydroanisoin	80
β -(<i>m</i> -Methoxybenzoyl)- α -anisylpro- pionic acid ^k	γ -(<i>m</i> -Methoxyphenyl)- α -anisylbuty- ric acid ^k	15

TABLE I REDUCTIONS WITH NICKEL-ALUMINUM ALLOY

^a The yields are based on the reduction of 10 g. of the carbonyl compound. ^b Also reduced with the aluminum-nickel catalyst combination. ^c 25 cc. of alcohol used as solvent. ^d Prepared p-nitrobenzoate, m.p. 80-81°; Cale'd. for $C_{22}H_{19}O_4N$:C, 73.10; H, 5.30. Found: C, 73.19; H, 5.70. ^e Also prepared by J. v. Braun and H. Deutsch, Ber., **45**, 2187 (1912), b.p., 205-210°/13 mm. The 1-(p-phenoxyacetic acid)-3-phenyl propane, m.p. 92-93°; Cale'd for $C_{17}H_{18}O_3$: C, 75.51; H, 6.72. Found: C, 75.25; H, 6.62. ^f 25 cc. of toluene used as solvent. ^a Also prepared by Borsche and J. Wollemann, Ber., **45**, 3719 (1912) Cale'd for $C_{34}H_{30}O_2$: C, 86.82; H, 6.06. Found: C, 86.57; H, 6.40%. ^b 4.4'-Dinitro derivative m.p. 179-180°, J. Am. Chem. Soc., **52**, 5041 (1930). ⁱAdditional 10 g. alloy yielded dibenzyl exclusively. ^j 25 cc. of alcohol and 25 cc. of toluene used as solvent. ^k Prepared by Robinson, et al, Proc. Roy. Soc., **B127**, 164 (1939).

further heating of the reaction mixture with the addition of 5 g. of alloy and 50 ml. of 10% sodium hydroxide gave indications of an increased yield, especially with the alkali-insoluble compounds. The hot solution was filtered and the residue was washed thoroughly with water in such a manner that it was always covered with fluid. If the nickel residue is allowed to become dry it will ignite. The filtrate was cooled and acidified to Congo red paper with concentrated hydrochloric acid. It is desirable to effect the acidification by

adding the alkaline solution to the hydrochloric acid with stirring. If the acidification is carried out in the reverse order, aluminum salts usually precipitate out and it is then necessary to heat the solution in order to redissolve the salts. The reduction product was isolated either by filtration or by extraction of the acidified solution. For the alkaliinsoluble compounds the reductions were carried out in a one-liter flask equipped with an adapter and reflux condenser. During the addition of the alloy the reaction mixture was shaken frequently. With several compounds, toluene was added in sufficient quantity to retain the compound in a uniform surface layer (3). Other compounds were reduced in the presence of an amount of alcohol sufficient to keep them in solution. The reduction product was isolated either by steam distillation or extraction of the alkaline solution.

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SUMMARY

1. The use of a nickel-aluminum alloy (Raney's) in aqueous alkali for the reduction of carbonyl compounds is described.

2. Carbonyl compounds of the general formula C_6H_5C =OR where R is hydrogen, alkyl, or anyl yield the corresponding hydrocarbon.

3. Carbonyl compounds of the general formula $C_{\delta}H_{\delta}(CH_2)_{x}C=OR$ or $C_{\delta}H_{\delta}CH=CH(CH_2)_{x}C=OR$ where R is hydrogen or alkyl yield the corresponding alcohol.

4. The reduction of alkali-soluble carbonyl compounds proceeds smoothly in good yield whereas the reduction of the alkali-insoluble carbonyl compounds proceeds satisfactorily in the presence of a solvent such as alcohol or toluene.

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