[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

RANEY NICKEL AS AN ORGANIC OXIDATION-REDUCTION CATALYST[1]

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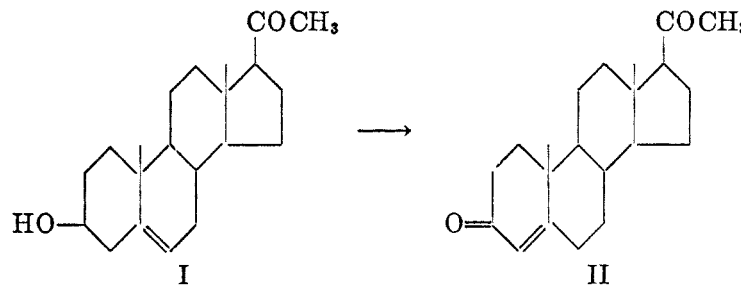
The versatility of Raney nickel as a catalyst in effecting various reductive transformations of organic compounds is quite well known (1, 2). Catalytic oxidations in the presence of Raney nickel, however, are relatively obscure (2, 11). Paul (3) and Palfrey (4), for example, have shown that certain secondary alcohols may be dehydrogenated catalytically to the corresponding ketones; however, temperatures up to 250° must be used, and even then yields leave much to be desired. A recent report (5) of work by H. Ruschig at the I. G. Farbenindustrie laboratories has described the catalytic conversion of pregnenolone (I) to pro-



gesterone (II) in the presence of a special Raney nickel catalyst and cyclohexanone as a hydrogen acceptor. The object of the present investigation was to determine the generality of this oxidation and to study the possibility of using it in the reverse sense; *i.e.*, as a reductive method in the presence of a hydrogen donor. The latter phase would constitute an extension of the work of Mozingo *et al.* (12).

Preliminary attempts to oxidize cholesterol to cholestenone using cyclohexanone as hydrogen acceptor showed that the special aerated Raney nickel as prepared by Ruschig (5) was considerably less effective than the usual Raney nickel kept under toluene. For this reason ordinary Raney nickel was employed in all the subsequent investigations. Cyclohexanone was used as hydrogen acceptor in the oxidations because of its favorable oxidation potential (6), and the method involved merely refluxing a mixture of the compound to be oxidized, with the hydrogen acceptor, and catalyst in toluene. Table I shows the variety of secondary alcohols which may be converted to the corresponding ketones by this procedure. The oxidation of cholesterol involves a simultaneous shift of the Δ^5 double bond to the Δ^4 position in conjugation with the carbonyl group. This shift occurs likewise in the usual Oppenauer oxidation of cholesterol (7).

[1] Since the completion of this work, related conversions by means of Raney nickel have been reported by Dubois (15).

When the redox reaction was next studied as a preparative reduction method, it was found that a wide variety of compounds could be reduced in the presence of any of several different potential hydrogen donors (see Table II). The types of conversion effected are similar to those brought about either by high pressure hydrogenation (1) or by the action of alkali on nickel-aluminum alloy (9). Carbonyl groups, activated ethylenic, and acetylenic bonds in varied environments are smoothly reduced. Hydrogenolysis of the carbon-oxygen bond occurs when α to an aromatic ring. Related reductions have been carried out by Bougault (11) and by Mozingo (12) with Raney nickel, the latter using ethanol as solvent. These workers believed that the hydrogen for reduction was supplied only by the catalyst and have not mentioned the possibility that the hydroxylic solvents employed may act as hydrogen donors. Support for this latter view has been

TABLE I

OXIDATIONS[a]

COMPOUND OXIDIZED	HYDROGEN ACCEPTOR	CATALYST, G./G. CPD.	HOURS REFLUX	PRODUCT ISOLATED	% YIELD
Cholesterol	Cyclohexanone	2.0	24	Cholestenone	80
Benzoin	"	2.0	24	Benzil	35
Benzhydrol	"	2.0	22	Benzophenone	30
Dihydrocholesterol	"	2.5	24	Cholestanone	80
Epicoprostanol (8)	"	1.5	24	Coprostanone	50
Fluorenol	"	2.5	24	Fluorenone	76

[a] Under the conditions of the oxidation xanthydrol gave a 30% yield of dixanthyl, m.p. 207–208°. This seems to be an anomalous case.

Anal. Calc'd for $C_{26}H_{18}O_2$: C, 86.16; H, 5.01.
Found: C, 85.96; H, 4.97.

obtained in the isolation of acetone (as its 2,4-dinitrophenylhydrazone) from reduction experiments in which isopropanol was used as hydrogen donor. Under similar conditions Wolfrom (13) has recently isolated acetaldehyde when using ethanol as solvent. It is thus probable that both the hydrogen donor and the hydrogen adsorbed on the catalyst play a part in these reductions, especially when only small amounts of catalyst are used. We have found, however, that in the presence of excess Raney nickel, stilbene may be reduced in 80% yield to dibenzyl when dioxane is used as solvent. It is evident, therefore, that reductions may be effected entirely by means of the hydrogen adsorbed on the catalyst. The rôle of the hydrogen donor solvents is thus an accessory one.

The identity of each product formed in the oxidations or reductions was established either by mixed melting point determinations with authentic samples or by analysis. The tables are largely self-explanatory.

EXPERIMENTAL

Preparation of the nickel catalyst. Raney nickel was prepared by the method of Mozingo (14), and after the exhaustive washing the water was decanted and toluene added. The

TABLE II

REDUCTIONS

COMPOUND REDUCED	HYDROGEN DONOR	CATALYST, G./G. CPD.	HOURS REFLUX	PRODUCT ISOLATED	% YIELD
Cholestanone	Cyclohexanol	2.0	22	Dihydrocholesterol	50
Coprostanone	"	2.0	22	Epicoprostanol	20
Benzoin	"	2.5	24	Dibenzyl[a]	58
Desoxybenzoin	"	2.5	24	"	20
Cholestenone	"	1.7	24	Dihydrocholesterol	10
Mesohydrobenzoin	"	1.6	24	Dibenzyl	17
Benzophenone	Diethylcarbinol	2.5	24	Diphenylmethane[b]	75
"	Isopropanol	3.0	31	"	36
Desoxyanisoin	Cyclohexanol	1.1	24	*p,p'*-Dimethoxydibenzyl[c]	80
Anisal-*p*-methoxyacetophenone	Diethylcarbinol	3.2	24	1,3-Di-*p*-methoxyphenylpropane[d]	80
Stilbene	"	3.4	24	Dibenzyl	60
Benzilic acid	Isopropanol	4.6	16	Diphenylmethane[e]	5
Laurone	"	2.5	23	Diundecylcarbinol	80
Ethyl *o*-benzoylbenzoate	"	3.2	19	*o*-Benzylbenzoic acid[f]	86
Diphenylacetylene	Ethanol	6.5	7	Dibenzyl	77
Di-[4,4'-tetramethyldiaminobenzhydryl] ether	Isopropanol	4.8	16	4,4'-Tetramethyldiaminodiphenylmethane	50
3-Acetylquinoline	"	5	24	3-Ethyl-5,6,7,8-tetrahydroquinoline[g]	62
9-Anthraldehyde	"	4	6	9-Hydroxymethylanthracene[h] +	10
				anthracene	10

[a] *Anal.* Calc'd for $C_{14}H_{14}$: C, 92.26; H, 7.74.
Found: C, 91.83; H, 7.88.

[b] Tetranitro derivative m.p. 170–172°.

[c] *Anal.* Calc'd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49.
Found: C, 78.63; H, 7.14.

[d] *Anal.* Calc'd for $C_{17}H_{20}O_2$: C, 79.65; H, 7.86.
Found: C, 79.48; H, 7.62.

[e] Most of the benzilic acid was recovered unchanged. The method of Schwenk and Papa (9) is superior for acidic compounds.

[f] Obtained by alkaline hydrolysis of the crude reduction product.

[g] Isolated as the picrate, m.p. 160–161.5° (10).
Anal. Calc'd for $C_{11}H_{15}N \cdot C_6H_3O_7N_3$: C, 52.31; H, 4.65.
Found: C, 52.41; H, 4.45.

[h] *Anal.* Calc'd for $C_{15}H_{12}O$: C, 86.50; H, 5.81.
Found: C, 86.92; H, 5.66.

toluene was then distilled until no further water was removed. The catalyst was stored under toluene.

Typical oxidation procedure. Oxidation of dihydrocholesterol. Toluene (150 ml.), cyclohexanone (50 ml.), Raney nickel (10 to 15 g.), and dihydrocholesterol (5 g.) were refluxed

with efficient stirring for 24 hours. The catalyst was filtered, and the toluene and cyclohexanone were removed by distillation *in vacuo*. The residue was taken up in ether, filtered, and the ether removed on a steam-bath. The product was recrystallized from ethanol, m.p. 127–129°; yield, 80%. Other oxidations were run in an exactly similar fashion.

Typical reduction procedure. Reduction of anisal-p-methoxyacetophenone. Toluene (125 ml.), diethylcarbinol (75 ml.), Raney nickel (15–16 g.), and anisal-*p*-methoxyacetophenone (5 g.) were refluxed with stirring for 24 hours. The catalyst was filtered, and the solvents were distilled *in vacuo*. The product was recrystallized from ethanol, m.p. 42–44°; yield, 80%. Further recrystallization raised the melting point to 45.0–45.5°. Reductions using cyclohexanol and diethylcarbinol as hydrogen donors were run exactly as this example except that digitonin precipitation was used to separate mixtures formed in reactions (2) and (5) (Table II). In those cases in which isopropanol or ethanol were used, toluene was omitted, and in its place extra donor solvent was substituted.

Reduction in absence of donor solvent. Reduction of stilbene. A mixture of stilbene (5 g.), dioxane (200 ml.), and Raney nickel (22 g.) was refluxed with stirring for 24 hours. The catalyst was filtered, and the filtrate was concentrated *in vacuo*. The product was recrystallized from methanol. Dibenzyl was thus obtained in 80% yield, m.p. 52.0–52.5°.

SUMMARY

1. Raney nickel in the presence of a hydrogen acceptor may be used to catalyze the oxidation of secondary alcohols to the corresponding ketones.

2. Reduction of the carbonyl group, ethylenic double bond, and acetylenic triple bond may likewise be effected by Raney nickel in the presence of a hydrogen donor. Hydrogenolysis of carbon-oxygen bonds α to aromatic nuclei has been observed.

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