[Contribution from the Research Laboratory of Merck & Co., Inc.]

Hydrogenation by Raney Nickel Catalyst without Gaseous Hydrogen

By Ralph Mozingo, Claude Spencer and Karl Folkers

Previous communications[1,2,3] have reported the hydrogenolysis of sulfur-containing compounds by Raney nickel catalyst in the absence of hydrogen except that contained in the catalyst. When such reactions are used in structure determinations on an unknown substance, it is useful to know their limitations. Because of this, a few types of compounds which do not contain sulfur have been subjected to similar treatment in order to observe additional reactions which may proceed simultaneously with the hydrogenolysis of carbon–sulfur bonds.

It has been reported that nitrobenzene is converted into a mixture of azobenzene and azoxybenzene by Raney nickel catalyst[4] and that ozonides are converted into aldehydes.[5] All of these reactions were run without gaseous hydrogen and since relatively small amounts of nickel were used, nickel is the main reactant and not its contained hydrogen. Recently, it was demonstrated that when sufficiently large amounts of Raney nickel catalyst were used the hydrogen in the catalyst is available for hydrogenation[6] of double bonds in organic acids. It is hydrogenation by this hydrogen contained in Raney nickel catalyst which is the basis for the present investigation.

Under the conditions used for the hydrogenolysis of sulfides,[1] it has now been found that carbon to carbon double bonds, carbonyls, azoxy and hydrazo linkages, and the like are reduced. Examples of these are the hydrogenation of the double bonds in benzalacetone, eugenol and cholesterol, and the carbonyl in acetone, ethyl acetoacetate, cyclopentanone and benzalacetone, and the hydrogenolysis of the azoxy linkage in azoxybenzene and of the hydrazo linkage in hydrazobenzene. Likewise, aromatic alcohols may be converted into the corresponding hydrocarbons (or derivatives) by hydrogenolysis; benzaldehyde gives toluene and not benzyl alcohol. However, benzene rings, aliphatic acids,[1] and esters are stable to reduction under these conditions.

It is evident that such reactions are all known[7] by the use of hydrogen together with small quantities of the catalyst. However, the low temperature at which some of the reactions proceed is unusual. For example, nitrobenzene is reduced and alkylated to give N-ethylaniline in three hours at 78°, about 100° below the usual temperature for alkylation of amines by alcohol.[8] Benzyl alcohols do not undergo hydrogenolysis at temperatures much below 100° with hydrogen and small amounts of Raney nickel catalyst.[9] But when treated with large amounts of the catalyst (without uncombined hydrogen), benzyl alcohol and benzaldehyde are converted into toluene at 78° in two hours. One example of the cleavage of a carbon to carbon bond in compounds of the type $RSCH_2CH_2SR$ to give methane as well as ethane has been reported.[3]

Experimental Part

Attempted Hydrogenation of Toluene.—Five grams of toluene, about 25 g. of Raney nickel catalyst, 100 ml. of ethyl alcohol and 35 ml. of water were refluxed for five hours on a steam-bath. The product was steam distilled twice, separated from the water and alcohol, and dried with calcium chloride. Its refractive index was $n^{29}D$ 1.4910. Since refractive index of the toluene used was $n^{29}D$ 1.4905, it was not reduced. Four grams was recovered (80%).

Hydrogenation of Cyclopentanone.—Five grams of cyclopentanone, about 25 g. of Raney nickel catalyst, 100 ml. of ethyl alcohol and 35 ml. of water were refluxed for two hours. The nickel was removed by filtration and the product extracted with benzene. The benzene and alcohol were carefully distilled through a fractionating column, the residue being taken as the reduction product. From half the residue and 7.0 g. of 3,5-dinitrobenzoyl chloride in pyridine, 5.1 g. of cyclopentyl 3,5-dinitrobenzoate was obtained (61%). The derivative was recrystallized several times from ethyl alcohol and melted at 115–116°.

Anal. Calcd. for $C_{12}H_{12}O_6N_2$: C, 51.43; H, 4.32; N, 10.00. Found: C, 51.56; H, 4.19; N, 10.10.

The remaining reduction product was converted into a *p*-nitrobenzoate which was recrystallized several times from ethyl alcohol. The melting point of the cyclopentyl *p*-nitrobenzoate was 61–62°.

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.27; H, 5.57; N, 5.96. Found: C, 61.56; H, 5.62; N, 6.01.

Hydrogenation of Hydrazobenzene.—Five grams of hydrazobenzene, about 25 g. of Raney nickel catalyst and 100 ml. of alcohol were refluxed for three hours. The nickel was removed, the solution acidified with sulfuric acid and the alcohol distilled. The residue was neutralized with sodium hydroxide, extracted with ether, and dried over potassium hydroxide. The hydrochloride of N-ethylaniline was precipitated by passing dry hydrogen chloride into the ether solution. After four recrystallizations from alcohol and ether, it melted at 173–175°. The melting point of N-ethylaniline hydrochloride is recorded[10] as 172–173°. The yield was 5.2 g. (43%).

Anal. Calcd. for $C_8H_{12}NCl$: C, 60.95; H, 7.68; N, 8.89. Found: C, 61.00; H, 7.95; N, 9.08.

Hydrogenation of Azoxybenzene.—Five grams of azoxybenzene, about 25 g. of Raney nickel catalyst and 100 ml. of alcohol were refluxed and treated in the same way as hydrazobenzene. The hydrochloride of the reduction product had the same melting point as the N-ethylaniline hydrochloride produced from hydrazobenzene, 173–175°,

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[1] Mozingo, Wolf, Harris and Folkers, This Journal, **65**, 1013 (1943).

[2] du Vigneaud, Melville, Folkers, Wolf, Mozingo, Keresztesy and Harris, *J. Biol. Chem.*, **146**, 475 (1942).

[3] Snyder and Cannon, This Journal, **66**, 155 (1944); Snyder, Howe, Cannon and Nyman, *ibid.*, **65**, 2211 (1943).

[4] Covert and Adkins, *ibid.*, **54**, 4116 (1932).

[5] Cook and Whitmore, *ibid.*, **63**, 3540 (1941).

[6] Bougault, Cattelain and Chabrier, *Bull. soc. chim.*, [5] **5**, 1699 (1938).

[7] Adkins, "Reactions of Hydrogen," the University of Wisconsin Press, Madison, Wis., 1937.

[8] Winans and Adkins, This Journal, **54**, 306 (1932).

[9] Ref. 7, p. 69.

[10] Reynolds, *J. Chem. Soc.*, **61**, 455 (1892).

and a mixed melting point of the two was 173–175°. The yield was 2.9 g. (36%).

Hydrogenation of Ethyl Acetoacetate.—Ten grams of ethyl acetoacetate, about 50 g. of Raney nickel catalyst and 150 ml. of ethyl alcohol were refluxed for five hours. The nickel was removed by centrifuging, the alcohol distilled, and the product distilled; b. p. 175–183°. The yield was 9.8 g. (96%). A sample of the product did not absorb any more hydrogen when subjected to hydrogenation under pressure, and did not form a 2,4-dinitrophenylhydrazone,[11] indicating that the ethyl acetoacetate was completely reduced to ethyl β-hydroxybutyrate. Saponification equivalent found was 133.7 (calcd. 132.2).

Hydrogenation of Benzalacetone.—Five grams of benzalacetone was refluxed with about 25 g. of Raney nickel catalyst and 100 ml. of ethyl alcohol for two hours, and the nickel removed by centrifuging. The alcohols were distilled and the product came over at 234°. The yield was 3.9 g. (75%).

The phenylurethan of the 4-phenyl-2-butanol, recrystallized from petroleum ether, melted at 114–115°. The melting point of this compound is given as 113°.[12]

Hydrogenation of Benzaldehyde.—Five grams of benzaldehyde, about 25 g. of Raney nickel catalyst and 100 ml. of alcohol were refluxed for two hours. The nickel was centrifuged from the solution and the product steam-distilled from the mixture. It measured 3.6 ml. (3.1 g., 78%) and was identified as toluene by its boiling point, 108–110°.

Hydrogenation of Acetone.—Five grams of acetone was refluxed with 25 g. of Raney nickel catalyst and 100 ml. of water for one and one-half hours. The nickel was centrifuged and the product distilled, along with some water. It was salted out with potassium carbonate; 4.9 cc. (4.0 g.; 78%).

The 3,5-dinitrobenzoate, recrystallized from ethyl alcohol, melted at 122–123°; the melting point of isopropyl 3,5-dinitrobenzoate is 123°.[13]

The product gave a negative test with 2,4-dinitrophenylhydrazine, indicating complete reduction.

Hydrogenation of Eugenol.—A solution of 2 g. of eugenol in 135 ml. of 70% ethyl alcohol was refluxed for five hours with about 25 g. of Raney nickel catalyst. The nickel and alcohol were removed. Benzene was added and removed by distillation in order to remove traces of ethyl alcohol. The residue gave 2.9 g. (75%) of dihydroeugenol p-nitrobenzoate, m. p. 73–74° (after crystallization from methanol).

Anal. Calcd. for $C_{17}H_{17}O_5N$: C, 64.75; H, 5.43; N, 4.44. Found: C, 64.78; H, 5.61; N, 4.59.

Hydrogenation of Cholesterol.—Three runs were made, using 2 g. of cholesterol, about 25 g. of Raney nickel catalyst and 100 ml. of ethyl alcohol, and refluxing for five hours. The nickel was removed, and the solution concentrated. Crystals came out on cooling the solution and were collected and dried. In the first two runs, the product melted at 123–129°; in the third run, at 117–121°. Recrystallization from ethyl alcohol did not change these melting points, and their long range indicates the presence of more than one compound. Because of the possibility of incomplete reduction, the crystals from the third run were refluxed in 100 ml. of alcohol with 15 g. of fresh Raney nickel catalyst for three hours. The crystals obtained melted at 117–121°. Since the product gave a positive test for unsaturation,[14] the reduction was not complete.

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Summary

1. Under the conditions used for the hydrogenolysis of sulfides, carbon to carbon double bonds, carbonyls, nitro groups, hydrazo and azoxy linkages are reduced. Likewise, benzyl alcohol gives toluene.

2. Benzene rings, acids and esters are stable to reduction by this procedure.

3. Alkylation of an amine by ethyl alcohol in the presence of Raney nickel catalyst at 78° has been observed.

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[11] Brady, *J. Chem. Soc.*, 756 (1931).

[12] Klages, *Ber.*, **37**, 2313 (1904).

[13] Bryant, THIS JOURNAL, **54**, 3758 (1932); Reichstein, *Helv. Chim. Acta*, **9**, 799 (1926).

[14] Liebermann, *Ber.*, **18**, 1803 (1885); Burchard, Inaugural Dissertation, Rostock, 1889; cf. *Chem. Zentr.*, **61**, 25 (1890).

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

A Novel Product from the Alkaline Hydrolysis of a Quaternary Ammonium Bunte Salt[1]

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Benzyldimethylphenylammonium S-benzylthiosulfate, first encountered as a product of the reaction of benzyldimethylphenylammonium chloride and sodium thiosulfate,[3] decomposes on mild treatment with aqueous alkali to form dimethylaniline, benzoic acid, benzyl sulfide and benzyl disulfide. Evidently part of the reactions which occur are similar to those observed earlier[4] in the alkaline hydrolysis of the metal salts of alkyl- and arylthiosulfates. Thus, sodium S-benzylthiosulfate[4a] gave benzoic acid, thiobenzoic acid and benzyl disulfide. In order to characterize other products of the present reaction, and in particular to learn the fate of the benzyl group in the cation of the salt, benzyldimethylphenylammonium S-p-bromobenzylthiosulfate has been subjected to the action of aqueous alkali. The various products which have been identified are shown in the equation.

$$[p\text{-}BrC_6H_4CH_2SSO_3]^- \, [C_6H_5CH_2N(CH_3)_2C_6H_5]^+ \xrightarrow{KOH} C_6H_5N(CH_3)_2 + p\text{-}BrC_6H_4CHO + p\text{-}BrC_6H_4CO_2K + (p\text{-}BrC_6H_4C_2H_2S)_2 + C_6H_5CH_2SCH_2C_6H_4Br(p) + C_{14}H_{12}S_2O_2BrK$$

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[1] This is the fifth communication on reactions of quaternary ammonium salts; for the fourth, see THIS JOURNAL, **66**, 350 (1944).

[2] Present address: the University of Pennsylvania, Philadelphia, Pa.

[3] Snyder and Speck, THIS JOURNAL, **61**, 668 (1939).

[4] (a) Price and Twiss, *J. Chem. Soc.*, **93**, 1395 (1908); **97**, 1175 (1910); (b) Baumgarten, *Ber.*, **63**, 1330 (1930).