was reduced to the corresponding alcohol in 99 minutes. The hydrogen continued to be absorbed, although much more slowly, and when reactivation with oxygen was occasionally made, it was possible to continue the reduction until practically 4 moles of hydrogen had been absorbed. The reaction yielded practically pure cyclohexyl-1-butanol-3 boiling at 115–116° (18 mm.); n_D^{17}, 1.466. In a similar manner with 0.5 g. of catalyst, 20.8 g. of benzal-acetophenone in 150 cc. of C. P. ethyl acetate was reduced in about 1300 minutes, with the absorption of practically 4 moles of hydrogen.

Summary

1. The catalysts obtained by the fusion of chloroplatinic acid or palladous chloride with sodium nitrate have been shown to be very efficient in the hydrogenation of four types of olefins. Their value in preparative experiments has been indicated.
2. A comparison of the relative activities of platinum and palladium in the reduction of olefins shows that the former is, in general, more efficient.
3. The effect of groups on the speed of reduction of olefins has been discussed.
4. The importance of purity of the compound being reduced has been shown.
5. The addition of ferrous salt does not accelerate the reduction of *pure* olefins.
6. The catalytic hydrogenation of all types of olefins probably occurs by 1,2 addition.

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[CONTRIBUTION FROM THE DEPARTMENTS OF PHARMACOLOGY AND TROPICAL MEDICINE, HARVARD MEDICAL SCHOOL]

THE NITRATION OF PARA-CARBOXY-PHENOXYACETIC ACID

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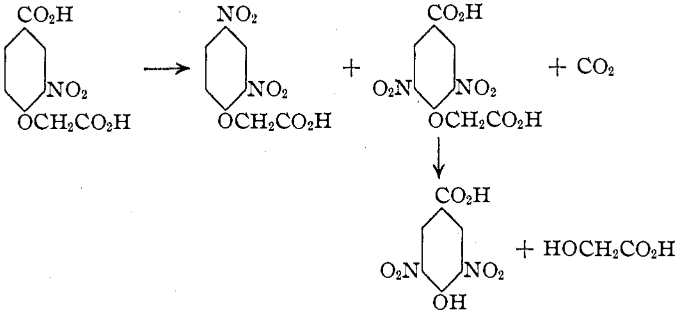
When *p*-carboxy-phenoxyacetic acid is treated with one molecular equivalent of nitric acid in the presence of sulfuric acid, 2-nitro-4-carboxyphenoxyacetic acid is formed practically quantitatively. The position of the nitro group is determined by conversion of the nitro acid into 3-nitro-4-hydroxybenzoic acid by hydrolysis with alkali; the hydrolysis product does not lower the melting point of a known specimen of 3-nitro-4-hydroxybenzoic acid prepared from *p*-hydroxybenzoic acid. When, however, two equivalents of nitric acid are used or when the mononitro compound is treated with one equivalent of nitric acid, the reaction proceeds in a rather unexpected direction, and carbon dioxide is evolved from the reaction mixture. The resulting material is not 2,6-dinitro-4-carboxy-phenoxyacetic acid but a mixture from which only 2,4-dinitro-phenoxyacetic acid and 3,5-dinitro-4-hydroxybenzoic acid can be isolated; the quantity of the latter is relatively small. The reaction may be expressed as follows.



The reaction products are separated by fractional crystallization from water and identified by analyses, by mixed-melting-point determinations with known specimens of 2,4-dinitro-phenoxyacetic acid and 3,5-dinitro-4-hydroxybenzoic acid prepared by nitration of phenoxyacetic acid[1] and *p*-hydroxybenzoic acid,[2] respectively, and in the case of the dinitro-phenoxyacetic acid by conversion into 2,4-dinitrophenol by hydrolysis with alkali.[3] In one experiment a small quantity of 2,6-dinitro-4-carboxy-phenoxyacetic acid was isolated.

Analogous instances in which a carboxyl group is replaced by a nitro group during nitration in sulfuric acid solution are the formation of various nitrophenols and nitro-anisoles as by-products when 3,5-dinitro-4-hydroxybenzoic acid and 3,5-dinitro-4-methoxybenzoic acid are prepared from *p*-hydroxybenzoic acid and anisic acid, respectively.[2a,2b,4] However, when nitric acid reacts with 2-nitro-4-carboxy-phenoxyacetic acid, the replacement of the carboxyl group is the main reaction, and the nitration of the nucleus is the side reaction.

That the 3,5-dinitro-4-hydroxybenzoic acid obtained in the present case is a secondary product the generation of which involves the primary formation of 2,6-dinitro-4-carboxy-phenoxyacetic acid is in keeping with the facts that a small quantity of the latter substance was isolated in one experiment and that phenoxyacetic acids of this type can be hydrolyzed very readily. Although phenoxyacetic acid itself requires comparatively

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[1] Pratesi, *Gazz. chim. ital.*, [2] **21**, 402 (1891).

[2] (a) Perkin, *J. Chem. Soc.*, **123**, 1025 (1898). (b) Salkowski, *Ann.*, **367**, 348 (1909). (c) Morgenstern, *Monatsh.*, **31**, 287 (1910).

[3] Pratesi [*Gazz. chim. ital.*, [1] **22**, 242 (1892)] showed that 2,4-dinitro-phenoxyacetic acid hydrolyzes readily forming dinitrophenol.

[4] (a) Reverdin, *Bull. soc. chim.*, [4] **3**, 591 (1908). (b) Salkowski and Rudolph, *Ber.*, **10**, 1255 (1877). (c) Diepolder, *Ber.*, **29**, 1756 (1896).

vigorous treatment in order to bring about hydrolysis, its nitro derivatives undergo hydrolysis more and more readily as the number of nitro groups increases.[3,5]

The yields of nitro-phenoxyacetic acids obtained by treating sodium nitrophenolates with sodium chloro-acetate in concentrated aqueous solution vary inversely with the ease of hydrolysis of the reaction product. Thus, the yields from *o*-nitrophenol, 2,4-dinitrophenol, and picric acid are 25%, 8% and 0%, respectively.[5] Consequently, the failure to obtain any reaction between the disodium salt of 3,5-dinitro-4-hydroxybenzoic acid and sodium chloro-acetate can be readily understood.

In attempting to alter the course of the reaction between 2-nitro-4-carboxy-phenoxyacetic acid and nitric acid, numerous variations in the experimental conditions were made. The results indicate, however, that whenever reaction occurs the products are those reported above.

p-Carboxy-phenoxyacetic acid has been prepared previously[5] by treating *p*-hydroxybenzoic acid with chloro-acetic acid in the presence of sodium hydroxide. In the present study the same reaction was employed but the experimental conditions were changed somewhat; the yield remained practically unchanged. Meyer and Duczmal did not recrystallize their product and reported the melting point as 278°. After recrystallization this substance melts at 280–282°.

The accepted melting point for phenoxyacetic acid seems to be 96°, but Mamili, Gambetta and Rimimi[6] report finding 99–100°. The results obtained in this Laboratory confirm the latter value.

Experimental Part

***p*-Carboxy-phenoxyacetic Acid.**—A solution of 69 g. of *p*-hydroxybenzoic acid (0.5 mole) and 47.3 g. of chloro-acetic acid (0.5 mole) in 600 cc. of water containing 60 g. of sodium hydroxide (1.5 mole) is refluxed for three hours. The reaction mixture is made acid to congo red with hydrochloric acid and chilled. The white precipitate is washed, dried and recrystallized from alcohol. *p*-Carboxy-phenoxyacetic acid (40.5 g.) is obtained as a white, microcrystalline solid; m. p., 280–282°.

Anal. Calcd. for $C_9H_8O_5$: C, 55.1; H, 4.11. Found: C, 54.7; H, 4.40.

An additional 19.6 g. of material, m. p. 275–280°, and 15.5 g. of unchanged *p*-hydroxybenzoic acid can be obtained by evaporation of the alcoholic mother liquor.

2-Nitro-4-carboxy-phenoxyacetic Acid.—Ten g. of 4-carboxy-phenoxyacetic acid is dissolved in 40 cc. of sulfuric acid and the solution treated with a mixture of 3.25 cc. of nitric acid (d., 1.42) and 3.25 cc. of sulfuric acid at —5° to 0° during mechanical stirring. After the nitrating acid has been added, the temperature is allowed to rise to 10° and the reaction mixture is diluted with 80 g. of ice and 80 cc. of water. After several hours, the white solid is collected on a filter, washed and dried at 80°. The crude product is recrystallized from 450 cc. of water; 10.6 g. of 2-nitro-4-carboxy-phenoxyacetic acid is obtained as feathery needles that are practically white; m. p., 247–248.5°. This sub-

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[5] Meyer and Duczmal, *Ber.*, **46**, 3366 (1913).

[6] Mamili, Gambetta and Rimimi, *Gazz. chim. ital.*, [1] **50**, 166 (1920).

stance is insoluble in ether, chloroform, and cold water, but soluble in alcohol and hot acetic acid; it dissolves in dil. alkali forming a yellow solution.

Anal. Calcd. for $C_9H_7O_7N$: N, 5.8. Found: 6.3.

HYDROLYSIS.—Three g. of this nitro compound is added to 20 cc. of 6 *N* sodium hydroxide solution; a large proportion of the resulting sodium salt remains undissolved. The mixture is heated in a beaker on a water-bath for two hours; the volume decreases to about 10 cc. and practically all the precipitate dissolves. The red solution is diluted with 30 cc. of water and acidified to congo red with hydrochloric acid. After the precipitate has been washed and dried, 1.6 g. of slightly impure 3-nitro-4-hydroxybenzoic acid is obtained as a buff-colored powder; m. p., 177–180°. When this material is recrystallized from 200 cc. of water, very fine needles are obtained which when mixed with a specimen prepared by nitration of *p*-hydroxybenzoic acid, did not lower the melting point.

Nitration of 2-Nitro-4-carboxy-phenoxyacetic Acid.—A solution of 5 g. of 2-nitro-4-carboxy-phenoxyacetic acid in 20 cc. of sulfuric acid is stirred and treated at 2° to 3° with a mixture of 1.32 cc. of nitric acid (d., 1.42) and 2.38 cc. of sulfuric acid. After the nitrating acid has been added, the cooling bath is removed and the reaction mixture which is stirred continuously is allowed to warm to room temperature. Soon, the evolution of carbon dioxide commences, and the solution becomes full of bubbles; this continues for some time. At the end of four hours the clear solution is diluted with 40 g. of ice and 40 cc. of water and left in the ice box overnight. The crude product (4.3 g.) after drying at 80° melts to a turbid liquid at 139–140° which becomes clear at 160°.

By dissolving this mixture in 100 cc. of hot water and cooling to room temperature 2.4 g. of crude 2,4-dinitro-phenoxyacetic acid is obtained as slightly yellowish, stout needles (m. p., 142–147°) which when recrystallized from 40 cc. of water yield 2.1 g. of pure material (m. p., 145–148°). When the latter is added to a specimen (m. p., 147–149°) of 2,4-dinitro-phenoxyacetic acid prepared from phenoxyacetic acid, the mixture melts at 146–148°.

Anal. Calcd. for $C_8H_6O_7N_2$: C, 39.7; H, 2.48; N, 11.6. Found: C, 39.0, 39.2; H, 2.66, 2.81; N, 11.9, 12.3.

In order to hydrolyze the dinitro-phenoxyacetic acid, 3 g. of the material is dissolved in 30 cc. of water and 4 cc. of saturated aqueous sodium carbonate, and the pale yellow solution is poured into 50 cc. of 10 *N* sodium hydroxide solution; a voluminous precipitate forms. After having stood in the ice box for several hours the solid is separated by centrifuging, washed successively with 7 *N* sodium hydroxide solution, a mixture of 7 *N* aqueous sodium hydroxide and alcohol, and finally with alcohol. The residual, moist solid is dissolved in about 40 cc. of hot water, and the solution is acidified with hydrochloric acid. The precipitate (1.2 g.) is 2,4-dinitrophenol (m. p., 112–113.5°).

When the mother liquor from the crude dinitro-phenoxyacetic acid is evaporated to a volume of about 25 cc., stout, prismatic crystals commence to separate from the hot solution. After several hours at room temperature, some finely divided precipitate commences to form; the coarse crystals are immediately collected, washed and dried. Recrystallization of the crude material (0.6 g.) from 75 cc. of water yields 0.45 g. of 3,5-dinitro-4-hydroxybenzoic acid as large, transparent, yellow plates that melt at 240.5–243° with slight preliminary softening at 230–235°. The melting point of this dinitro-hydroxybenzoic acid has been reported as 235–237°, 242–243°, 245–246°, and 248.5–249.5°. A specimen prepared by nitration of *p*-hydroxybenzoic acid was found to melt at 241–245° with preliminary softening at 236–237°; after the material had been dried for 20 hours at 107° the preliminary softening did not occur. A mixture of the yellow plates and the known material melts at 240–244° with preliminary softening at 230–236°.

Anal. Calcd. for $C_7H_4O_7N_2$: N, 12.3. Found: 12.5.

On standing in the ice box for seven hours the filtrate from the crude dinitro-hydroxybenzoic acid deposits a pale yellow, crystalline powder that is collected and dried. The product (0.55 g.) is a mixture of the two substances reported above and yields 0.38 g. of slightly impure dinitro-phenoxyacetic acid when recrystallized from water.

The mother liquor from the pale yellow, crystalline powder deposits 0.01 g. of crude dinitro-hydroxybenzoic acid when left in the ice box overnight. When the filtrate from the latter is evaporated to dryness, 0.6 g. of a sticky, yellow residue is obtained.

Nitration of *p*-Carboxy-phenoxyacetic Acid.—When a solution of 10 g. of *p*-carboxy-phenoxyacetic acid in 40 cc. of sulfuric acid is mechanically stirred and treated with a mixture of 8.1 cc. of nitric acid (d., 1.42) and 8.1 cc. of sulfuric acid at 10–20°, the evolution of carbon dioxide commences when about half of the nitrating acid has been added. After the addition of the acid, the temperature is raised to 30° and maintained at 30–35° for one hour; the solution is diluted with 40 g. of ice and 120 cc. of water. The crude product (12 g.) yields 10.3 g. of slightly impure 2,4-dinitro-phenoxyacetic acid.

An extensive fractionation of this material yields pure 2,4-dinitro-phenoxyacetic acid, some 2,4-dinitrophenol (formed by hydrolysis of the preceding substance) and 0.25 g. of 2,6-dinitro-4-carboxy-phenoxyacetic acid. The latter consists of very pale yellow leaflets; m. p., 182–183°.

Anal. Calcd. for $C_9H_6O_9N_2$: N, 9.8. Found: 10.1.

The expenses necessary for the pursuance of this investigation have been met in part from a fund for research in the Department of Tropical Medicine, given by a citizen of Boston.

Summary

1. When *p*-carboxy-phenoxyacetic acid is nitrated in sulfuric acid solution with one molecular equivalent of nitric acid, an excellent yield of 2-nitro-4-carboxy-phenoxyacetic acid is obtained.

2. When, however, two equivalents of nitric acid are used or when the mononitro compound is treated in sulfuric acid solution with one equivalent of nitric acid, the reaction products are 2,4-dinitro-phenoxyacetic acid and 3,5-dinitro-4-hydroxybenzoic acid. The latter is obtained only in small quantities and probably results from the hydrolysis of 2,6-dinitro-4-carboxy-phenoxyacetic acid.

3. The melting points of phenoxyacetic acid and *p*-carboxy-phenoxyacetic acid have been found to be 99–100° and 280–282°, respectively, instead of 96° and 278° as previously reported.

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