# Notes

## Hydrogenation of Pyridinecarboxylic Acids with Platinum Catalyst

MORRIS FREIFELDER

*Organic Chemistry Department, Research Division, Abbott Laboratories, North Chicago, Illinois*

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The inhibiting effect of the pyridine nitrogen and the more basic piperidino nitrogen on the catalyst during hydrogenation is well known.[1] It has been shown that the pyridine compound must be present as a salt or that hydrogenation of the base must be carried out in acidic medium to overcome this catalyst poisoning.[2]

In some recent work in this laboratory[3] we found that uptake of hydrogen proceeded smoothly during conversion of the isomeric pyridinecarboxylic acids in water in the presence of rhodium catalyst. While the yield of 3-piperidinecarboxylic acid was low due to decarboxylation, nevertheless the theoretical amount of hydrogen was absorbed.

Since the carboxyl group should in effect tend to neutralize the inhibitory effect of the basic piperidino nitrogen, it appeared to be of interest to attempt hydrogenation of the same acids with platinum oxide in a neutral medium.

Low pressure reductions were indeed successful with picolinic and isonicotinic acids. Nicotinic acid underwent decarboxylation during hydrogenation as observed by us with rhodium and previously with ruthenium catalyst.[4] In this work, however, uptake of hydrogen was never more than 35% of theory, and only piperidine and starting material were obtained.

The neutralizing effect of the carboxy group was enhanced by the shielding effect in 2-position, picolinic acid being completely reduced in four to five hours compared to isonicotinic acid which was only 50% complete in the same length of time.

This study would suggest then that pyridines containing a carboxyl group, such as the isomeric pyridylacetic acids, could be hydrogenated with platinum oxide catalyst, eliminating the use of the acid medium so necessary with other pyridines.

### Experimental

**Piperidine-2-carboxylic Acid.**—A mixture of 12.3 g. (0.1 mole) of picolinic acid in 150 cc. of water was hydrogenated under 2.5 atm. in the presence of 0.25 g. of platinum oxide. Uptake of hydrogen was complete in 4–5 hr. The solution was filtered and concentrated to dryness. The residue was then treated with absolute alcohol and filtered. On drying 12.7 g. (97%) of material was obtained; It melted at 276°.[5] A mixed melting point with an authentic sample was not depressed.

Piperidine-4-carboxylic acid was obtained in the same manner. Uptake of hydrogen was about 50% in 4–5 hr., but was complete in less than 18 hr. Yield of product melting at 336°[6] was 81.5%. A mixed melting point with isonicotinic acid (m.p. 317°) caused a drop to 230–240°, while a mixed melting point with an authentic sample was not depressed.

**Hydrogenation of Nicotinic Acid.**—Reduction was carried out in the same manner. However, uptake of hydrogen was about 35%, whether the reaction was carried out at room temperature or at 60°. The mixture was made basic and filtered. The alkaline solution was steam distilled into aqueous hydrochloric acid. The acid solution was then concentrated and the solid isolated. It weighed 2.0 g. (18%) and was identified as piperidine hydrochloride by its melting point and infrared spectrum. The alkaline solution after steam distillation was neutralized to pH 4.1 to recover nicotinic acid.

(1) E. B. Maxted and A. P. Walker, *J. Chem. Soc.*, 1093 (1948).
(2) T. S. Hamilton and R. Adams, *J. Am. Chem. Soc.*, **50**, 2260 (1928).
(3) M. Freifelder, R. M. Robinson, and G. R. Stone, *J. Org. Chem.*, **27**, 284 (1962).
(4) M. Freifelder and G. R. Stone, *ibid*, **26**, 3805 (1961).
(5) R. Willstätter, *Ber.*, **29**, 389 (1896), gives 274.5–275.5°.
(6) K. Freudenberg, *ibid.*, **51**, 1668 (1918), reports 325°.

## C-6 Hydroxylated Steroids. III. A New Preparative Method[1]

JOHN P. DUSZA, J. P. JOSEPH, AND SEYMOUR BERNSTEIN

*Organic Chemical Research Section, Lederle Laboratories, a Division of American Cyanamid Company, Pearl River, New York*

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Current interest in metabolites having a C-6 hydroxyl function[2] has stimulated our efforts to establish a facile chemical approach to the synthesis of these compounds.

We have previously outlined a preparation of 9α-fluoro-6β,11β,17α,21-tetrahydroxypregn-4-ene-3,20-dione[3] which comprised the reaction of 21-acetoxy-9α-fluoro-11β,17α-dihydroxypregn-4-ene-3,20-dione with trimethyl orthoformate to yield the crude $\Delta^{3,5}$-methyl enol ether. The latter

(1) For the previous paper in this series see, R. Littell and S. Bernstein, *J. Org. Chem.*, **27**, 2544 (1962).
(2) Leading references have been collected in ref. 1.
(3) L. L. Smith, J. J. Goodman, H. Mendelsohn, J. P. Dusza, and S. Bernstein, *J. Org. Chem.*, **26**, 974 (1961).