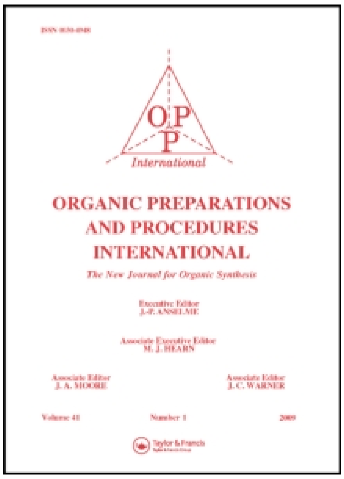

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# 3,5-PYRIDINEDICARBOXYLIC ACID (Dinicotinic acid)

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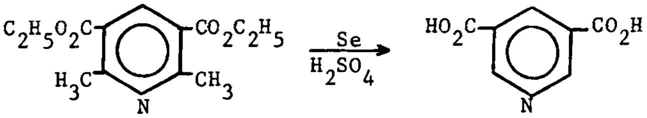

In connection with another study, we required a substantial quantity of bispidine (3,7-diazabicyclo[3.3.1]nonane) which is a direct precursor to 1,3-diazaadamantanes and a selective complexing agent.[1,2] The various procedures available for the preparation of bispidine are relatively low-yield and/or inconvenient.[1-4] Of these, the method of Stetter and co-workers[1,2] appeared to be the one of choice. Their procedure, however, suffers from a low-yield (30-40%), time consuming, inconvenient first step involving the oxidative decarboxylation of 3,5-dicarbethoxy-2,6-lutidine[5] to dinicotinic acid, using a very cumbersome quantity (13ℓ) of 6% aqueous potassium permanganate.[1,6] Since this reaction was really the only deficiency in the multistep synthetic scheme, it was our intention to find a more efficient, rapid, and less tedious method for the aforementioned conversion.

We have found that this conversion can be effected in good yield (60-75%) by employing selenium in conc. sulfuric acid.[7,8] The reaction and the work-up can be carried out in a short period of time and the product isolated with ease.

Finally, it should be noted that oxidative decarboxylation using selenium in sulfuric acid has received little recognition in the chemical literature although it appears to be a general and efficient technique.

## EXPERIMENTAL[9]

3,5-Pyridinedicarboxylic acid. A 3ℓ. one-neck flask with a thermometer cavity was fitted with a heating mantle and a thermometer. It was charged with crude, dry 3,5-dicarbethoxy-2,6-lutidine (167.7 g, 0.67 mole),[5] selenium powder (100 g), and 750 ml of conc. sulfuric acid, swirled gently, and fitted for distillation. The mixture was heated (*ca.*10°/min). Gas evolution began when the reaction mixture reached *ca.* 110°C and a liquid began to distill at *ca.* 160°C. Heating was continued until the pot temperature was between 280° and 300°C (*ca.* 2 hrs. total heating time). Approximately 300 ml of distillate was collected. The mixture was cooled to room temperature and poured into 2.0ℓ of cold water. The apparatus was rinsed with ~200 ml of water[10] and the combined aqueous solution filtered with suction. The filtrate was neutralized with 50% w/w aqueous sodium hydroxide, heated on a steam bath with 10 g of activated carbon (Norit-A), filtered warm with suction, and acidified to *ca.* pH = 3 (pHydrion paper or Thymol blue) with conc. hydrochloric acid. The mixture was well cooled in ice and the precipitated solid was filtered with suction. The tan product was washed with *ca.* 250 ml of ice water and dried in an oven at 100°C. The yield of light brown, powdery, diacid was 84.5 g (75%) mp. 323° (dec.).[11] The product is sufficiently pure[12] for most synthetic uses including the next step enroute to bispidine.[1,2]

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5. This material may be easily prepared in large quantities. See A. Singer and S. M. McElvain, Org. Syn., Coll. Vol. II, 214; B. E. Norcross, G. Clement, and M. Weinstein, J. Chem. Ed., 46, 694 (1969).

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9. (a) Selenium is a very poisonous substance and it should be handled with care. (b) The reaction should be carried out in a good hood. (c) Red amorphous selenium "steam distills" and coats distillation equipment during the course of the reaction. It may be removed by treatment with conc. nitric acid (in a hood).

10. A mass of fused selenium remained in the reaction vessel. It may be recovered, but we found it convenient to dissolve it in conc. nitric acid.

11. Handbook of Chemistry and Physics, p. C-502, The Chemical Rubber Co., 47th edition reports a melting point of 323° with decomposition.

12. Further purification was deemed unnecessary. The nmr spectrum of the product in dimethyl sulfoxide-$d_6$ with sodium 3-trimethylsilylpropane sulfonate as an internal reference revealed no unexpected peaks; nmr (in ppm), 8.80 (triplet, 1H), 9.40 (doublet, 2H), 10.8 (broad singlet, 2H).

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