

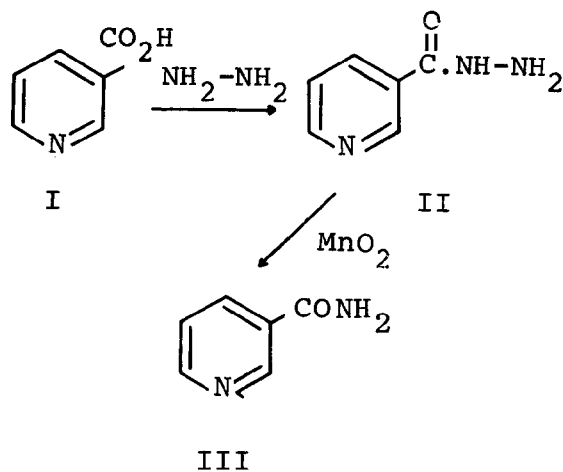
Synthesis of Nicotinamide

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Several methods for the synthesis of nicotinamide are reported in the literature¹⁻⁷. Some of these methods¹⁻⁴ require the use of 3-cyanopyridine as the starting material which is difficult to prepare. A method reported for the preparations of nicotinamide from nicotinic acid required the esterification of nicotinic acid followed by reaction of the ester with ammonia for twenty four hours⁵. A direct autoclave reaction of nicotinic acid with ammonia at 223° also yielded nicotinamide⁶. Nicotinamide has also been prepared⁷ by the catalytic hydrogenolysis of nicotinic acid hydrazide. We now wish to report a simple more convenient and efficient method for the preparation of nicotinamide from nicotinic acid. The method consists of conversion of nicotinic acid (I) to its hydrazide (II) followed by the reaction of hydrazide (II) with manganese dioxide and is represented by the Scheme.



Scheme.

Nicotinic acid hydrazide (II) was prepared by refluxing a mixture of nicotinic acid (I, 10 g) and hydrazine hydrate (40%, 50 ml) for three hours. After this period of time, the reaction mixture was cooled and filtered. The crude solid was recrystallised from methanol to yield white crystals of nicotinic acid hydrazide (II, 9.2 g, 82%), m.p. 160-161°, lit⁸. m.p. 161-162°.

Nicotinamide (III) was conveniently prepared by refluxing a mixture of II (5 g), manganese dioxide (35 g) and chloroform (200 ml) for three hours. After the reflux period was over, the reaction mixture was filtered while hot. The inorganic residue was boiled with two 50-ml portions of the solvent and filtered. Removal of the solvent from the combined filtrates yielded the crude nicotinamide as a light yellow solid. The crude solid was recrystallised from chloroform to yield needle like fine crystals of nicotinamide (III, 2.8 g, 62%), m.p. 128-129°, lit.⁹ m.p. 129-130°, methiodide of (III), m.p. 204°, lit.¹⁰ m.p. 204°.

Further work on the synthesis of some other amides from their corresponding acids by this method is in progress.

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