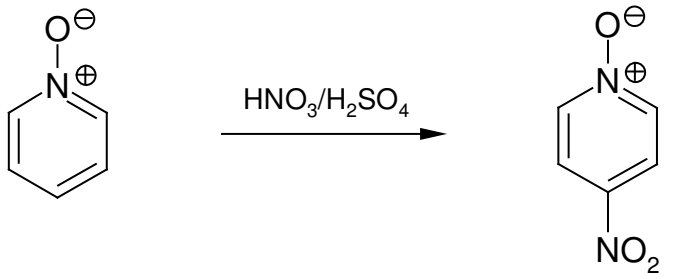
1004 Nitration of pyridine-N-oxide to 4-nitropyridine-N-oxide



C_5H_5NO			$C_5H_4N_2O_3$
(95.1)	(63.0)	(98.1)	(140.1)

Classification

Reaction types and substance classes
electrophilic substitution of aromatics, nitration
aromatics, nitroaromatics, heteroaromatics

Work methods
stirring with magnetic stir bar, heating under reflux, adding dropwise with an addition funnel, filtering, evaporating with rotary evaporator, draining of gases, working with wash bottles, use of an ice cooling bath, heating with oil bath

Instruction (batch scale 100 mmol)

Equipment
100 mL three-neck flask, 250 mL Erlenmeyer flask, internal thermometer, reflux condenser, adapter with ground glass joint and hose coupling, addition funnel with pressure balance, 1 L beaker, heatable magnetic stirrer, magnetic stir bar, Buechner funnel, suction flask, 2 wash bottles, rotary evaporator, desiccator, ice bath, oil bath

Substances

pyridine-N-oxide (mp 61-64 °C)	9.51 g (100 mmol)
sulfuric acid (conc.)	30 mL (0.56 mol)
fuming nitric acid	12 mL (0.29 mol)
sodium carbonate decahydrate	about 100 g (for 180 mL saturated aqueous solution)
sodium hydroxide solution (2 M)	about 100 mL
acetone (bp 56 °C)	
ice	150 g

Reaction

Preparation of the nitrating acid: 12 mL (0.29 mol) fuming HNO_3 are filled in a 250 mL Erlenmeyer flask with magnetic stir bar. Slowly and in portions 30 mL (0.56 mol) conc. H_2SO_4 are added under stirring and cooling in an ice bath. The nitrating acid is brought to a temperature of 20 °C.

The reaction apparatus consists of a 100 mL three-neck flask with magnetic stir bar, reflux condenser, internal thermometer and addition funnel with pressure balance. The reflux condenser is equipped with an adapter with ground glass joint and hose coupling which is connected with a tube to drain the nitrous fumes, formed during reaction. The tube is connected with an empty safety wash bottle and this one is connected with a wash bottle containing about 100 mL aqueous 2 m NaOH solution.

9.51 g (100 mmol) pyridine-N-oxide are filled in the reaction flask and heated to 60°C. The nitrating acid is transferred into an addition funnel and added dropwise within 30 minutes under stirring without further heating. Thereby the internal temperature drops to about 40°C. Afterwards the reaction mixture is heated for 3 hours to 125-130°C internal temperature.

Work up

After cooling down to room temperature the reaction mixture is poured in a 1 L beaker containing 150g finely crunched ice. Then about 170 mL of a saturated sodium carbonate solution are added carefully in portions (strong foaming) until a pH-value of 7 - 8 is reached. A yellow crystalline solid precipitates, consisting of product and sodium sulfate. The precipitation is sucked off over a Buechner funnel, the aqueous filtrate is disposed.
Crude yield: 7.7 g

To the yellow crude product acetone is added and the insoluble white salt is separated over a Buechner funnel. The solvent is evaporated from the filtrate at a rotary evaporator, the remaining yellow product is dried in a desiccator.
Yield: 5.87 g (41.9 mmol, 42%); mp 157 °C

If necessary, the product can be recrystallized from acetone.

Waste management

Recycling

The evaporated acetone is collected and redistilled.

Waste disposal

Waste	Disposal
aqueous filtrate	solvent water mixtures, halogen free
filter residue of salt	solid waste, free from mercury
washing solution from the wash bottle	aqueous waste, alkaline

Time

6-7 hours, without drying

Break
Before work up
Before addition of acetone

Degree of difficulty
Easy

Instruction (batch scale 10 mmol)

Equipment
50 mL three-neck flask, 25 mL Erlenmeyer flask, internal thermometer, reflux condenser, adapter with ground glass joint and hose coupling, addition funnel with pressure balance, 400 mL beaker, heatable magnetic stirrer, magnetic stir bar, Buechner funnel, suction flask, 2 wash bottles, rotary evaporator, desiccator, ice bath, oil bath

Substances

pyridine-N-oxide (mp 61-64 °C)	951 mg (10.0 mmol)
sulfuric acid (conc.)	3.0 mL (56 mmol)
fuming nitric acid	1.2 mL (29 mmol)
sodium carbonate decahydrate	about 17 g (for 30 mL saturated aqueous solution)
sodium hydroxide solution (2 M)	about 50 mL
acetone (bp 56 °C)	
ice	30 g

Reaction
Preparation of the nitrating acid: 1.2 mL (29 mmol) fuming HNO_3 are filled in a 25 mL Erlenmeyer flask. Slowly and in portions 3.0 mL (56 mmol) conc. H_2SO_4 are added under slewing and cooling in an ice bath. The nitrating acid is brought to a temperature of 20 °C.

The reaction apparatus consists of a 50 mL three-neck flask with magnetic stir bar, reflux condenser, internal thermometer and addition funnel with pressure balance. The reflux condenser is equipped with an adapter with ground glass joint and hose coupling, which is connected with a tube to drain the nitrous fumes formed during reaction. The tube is connected to an empty safety wash bottle and this is connected with a wash bottle, containing about 50 mL aqueous 2 M NaOH solution.

951 mg (10.0 mmol) pyridine-N-oxide are filled in a reaction flask and heated to 60°C. The nitrating acid is transferred into an addition funnel and added dropwise within a few minutes under stirring without further heating. Thereby the internal temperature drops to about 40°C. Afterwards the reaction mixture is heated for 3 hours to 125-130 °C internal temperature.

Work up

After cooling down to room temperature the reaction mixture is poured in a 400 mL beaker, containing 30 g finely crunched ice. Then about 30 mL of a saturated sodium carbonate solution are added carefully in portions (strong foaming) until a pH-value of 7-8 is reached. A yellow crystalline solid precipitates, consisting of product and sodium sulfate. The precipitation is sucked off over a Buechner funnel, the aqueous filtrate is disposed.

To the yellow crude product acetone is added and the insoluble white salt is separated over a Buechner funnel. The solvent is evaporated from the filtrate at a rotary evaporator, the remaining yellow product is dried in a desiccator.
Yield: 700 mg (5.00 mmol, 50%); mp 156-157 °C

If necessary, the product can be recrystallized from acetone.

Waste management

Waste	Disposal
aqueous filtrate	solvent water mixtures, halogen free
filter residue of salt	solid waste, free from mercury
washing solution from the wash bottle	aqueous waste, alkaline

Time

6-7 hours, without drying

Break

Before work up
Before addition of acetone

Degree of difficulty

Easy

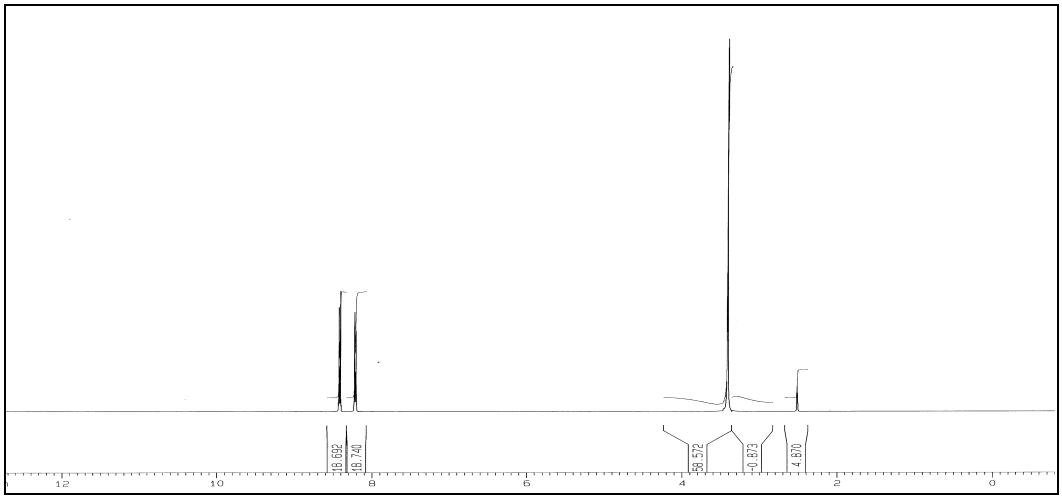
Analytics

TLC

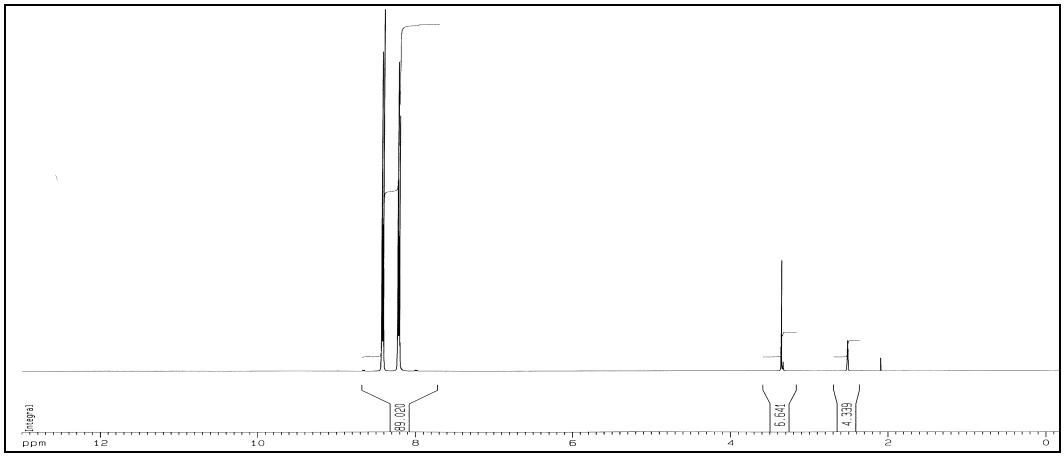
TLC-conditions:

adsorbant:	Macherey and Nagel Polygram SilG/UV foils, 0.2 mm
eluent:	dichloromethane: acetic acid ethyl ester = 5:3
R_f (product)	0.27
R_f (pyridine-N-oxide)	0.05

^{1}H NMR spectrum of the crude product (400 MHz, DMSO-D_6)

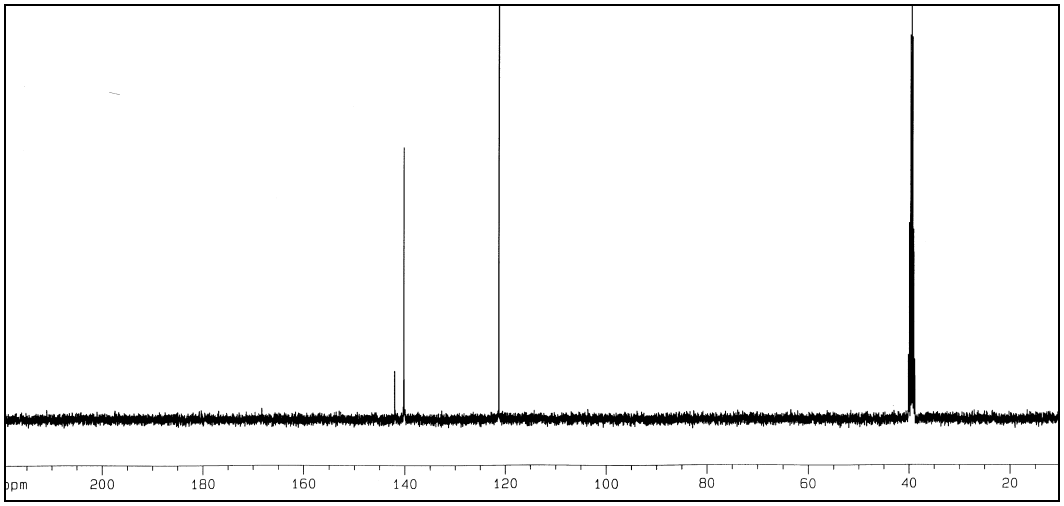


^{1}H NMR spectrum of the pure product (400 MHz, DMSO-D_6)



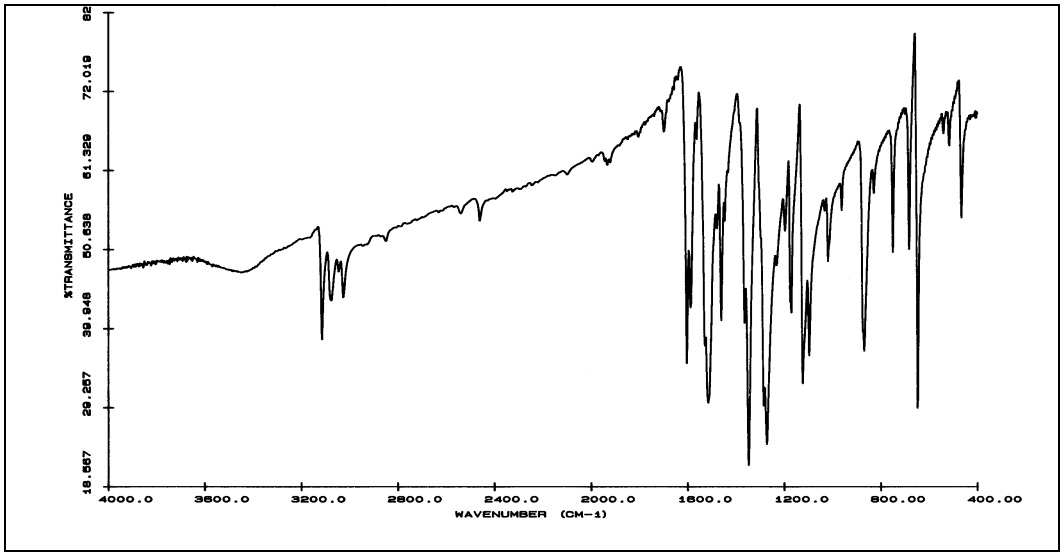
δ (ppm)	Multiplicity	Number of H	Assignment
8.18 - 8.23	m (AA')	2	2-H, 6-H
8.40 - 8.44	m (BB')	2	3-H, 5-H
3.3 and 2.5			water and DMSO
2.1			acetone

^{13}C NMR spectrum of the pure product (100 MHz, DMSO-D_6)



δ (ppm)	Assignment
121.31	C-3, C-5
140.20	C-2, C-6
142.01	C-4
39.5	solvent

IR spectrum of the pure product (KBr)



(cm^{-1})	Assignment
3115, 3080	C-H-valence, arene
1600	C=C-valence, arene,
1515, 1345	N=O-valence, asymm. and symm.