

1-Hydroxypyrazole (Large scale):

Pyrazole (90 g, 1.32 mole), ethyl acetate (6 L)¹ and m-chloroperbenzoic acid (70%, 360 g, 1.46 mole) were stirred for 7 d. Removal of the ethyl acetate by evaporation and drying overnight at 0.1 mmHg. The solid was extracted with water (ca. 300 mL and 4x200 mL) on a sintered glasfilter (Ø = 100 mm, G3)². The combined water-phases were evaporated to ca. 400 mL and extracted with CH₂Cl₂ (3 x 150 mL).³ The volume of the CH₂Cl₂ phase was reduced to ca. 100 mL and added conc. hydrochloric acid (100 mL)⁴. The organic phase was discarded and the aqueous phase was washed with dichloromethane (2 x 100 mL). The combined aqueous phases were added Na₃PO₄, 12H₂O (30 g) and pH was adjusted to 10.5⁵ by addition of 33% aqueous sodium hydroxide. Continuous extraction with diethyl ether for 24 h using a Kutchel-Stüdel apparatus⁶⁷ and removal of the solvents gave 32.4 g (36 %) of starting material. The pH of the aqueous solution was adjusted to ca. 2 by addition of conc. hydrochloric acid⁸. Continuous extraction⁹ with diethyl ether for 2 h¹⁰, replacement of the ether in the extraction flask and further extraction for 10 h. The ether extracts were combined and the ether removed to produce 55.5 g (50 %) of 1-hydroxypyrazole, m.p. 60-66 °C. Low temperature recystallisation (-78°C) from EtOAc (ca. 60 ml) gave m.p 70°C. (Reported m.p.75 °C). (Found: C, 42.78; H, 4.82; N, 33.58. C₃H₄N₂O requires C, 42.86; H, 4.80; N, 33.32 %).

¹ The reaction can be performed in two batches of 3 L.

² It is advised not to use too large volumes of water since the volume has to be reduced afterwards. It is important to disconnect the vacuum in between each extraction in order to get a sufficient "contact".

³ In order to remove trace amounts of m-chlorobenzoic acid

⁴ Backextraction is necessary because the first extraction with CH₂Cl₂ also removes some pyrazole and 1-hydroxypyrazole. Pyrazole and 1-hydroxypyrazole become protonated in conc. HCl and therefore remain in the aqueous phase.

⁵ At pH 10.5 pyrazole is on the neutral form whereas 1-hydroxypyrazole is present as its sodium salt (pKa of 1-hydroxypyrazole is 6.1).

⁶ The volume of the apparatus was ca. 750 mL. Often precipitation in the aqueous phase takes place after a while. Make sure that it doesn't block the tube leading ether into the aqueous phase.

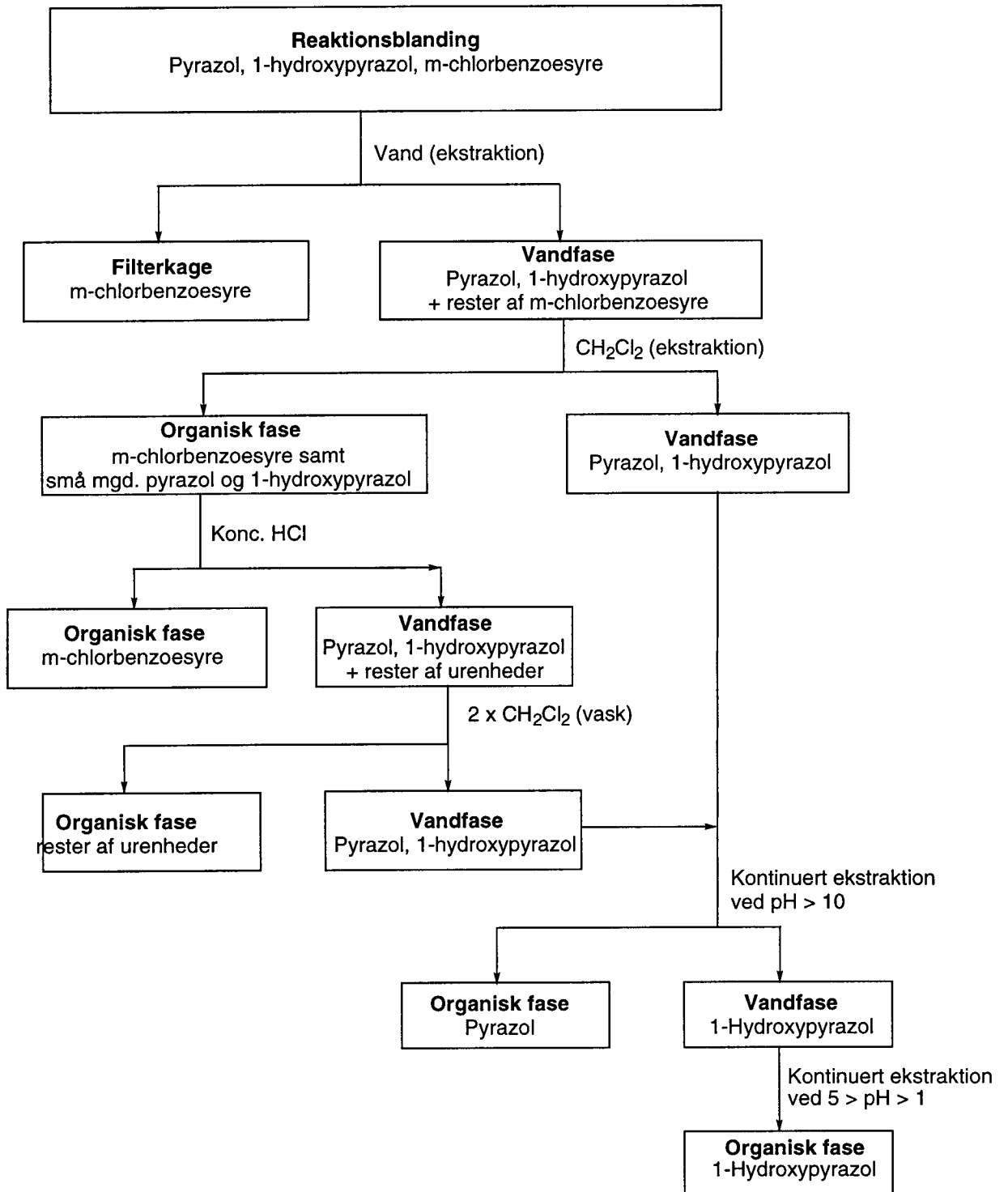
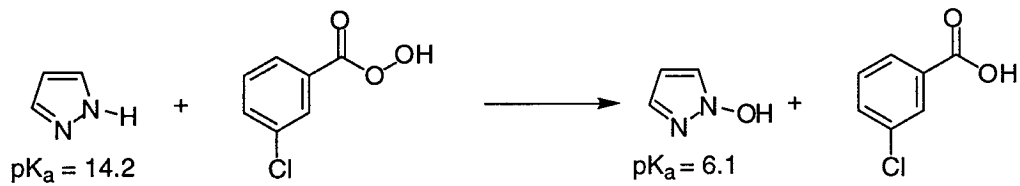
⁷ In order to avoid ignition of the ether when dripping onto the heating mantle it should be removed before the extraction flask is detached from the set up.

⁸ Conc. HCl (ca. 90 mL) can advantageously be added cautiously via the "long funnel".

⁹ See footnotes 6 and 7.

¹⁰ The first ether extract contains ca 80 % of the product obtained.

Udrystningskema fra oxidation af pyrazol



6/1/9 daga

Scant: CDC13
Ambient temperature
GEMINI-300BB "geminj"
PULSE SEQUENCE
Pulse 45.4 degrees
Acq. time 3.747 sec
Width 4500.5 Hz
32 repetitions
OBSERVE HI, 300.0673573 MHZ
DATA PROCESSING
FT size 65536
Total time 2 minutes

6.000-1

