Preparation and GC-MS-Identification of N-Methyl-Δ³-pyrroline

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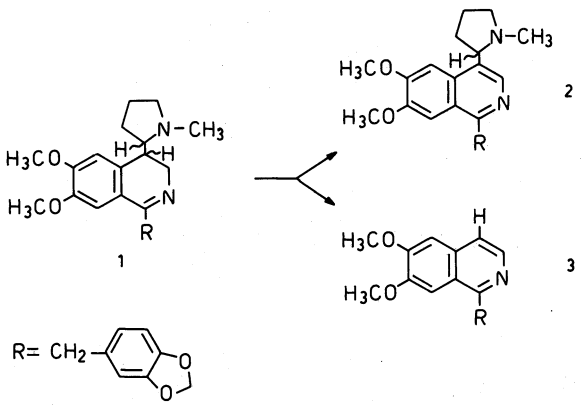
The preparation of N-methyl-Δ³-pyrroline by 1) reduction of N-methylpyrrole followed by gc-separation or by 2) condensation of cis-1,4-dichloro-2-butene with methylamine is described. The title compound is identified by GC-MS.

Darstellung und GC-MS-Untersuchungen an N-Methyl-Δ³-pyrrolin

Die Darstellung von N-Methyl-Δ³-pyrrolin 1) durch Reduktion von N-Methylpyrrol mit anschließender gc-Trennung und 2) durch Kondensation von cis-1,4-Dichlor-2-buten mit Methylamin wird beschrieben. Die Titelverbindung wird durch GC-MS identifiziert.

In the course of our synthesis of rac. macrostomine **(2)**[1] the last step comprises a Pd/C-catalyzed dehydrogenation of the 3,4-dihydroisoquinoline **1** (solvent: tetralin). **1** lost unexpectedly the N-methylpyrrolidine group under formation of the 1-benzylisoquinoline **3**[2] and minor amounts of **2**.



Later *Kapil* et al.[3] observed the same phenomenon in their synthesis of **2**.

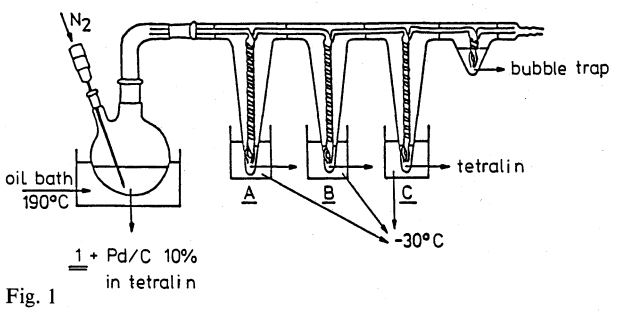


Fig. 1

In order to find out what had happened to the N-methylpyrrolidine moiety during the reaction mentioned above, we connected the reaction vessel containing **1**, Pd/C, and tetralin to a special trapping device (Fig. 1) for collecting possible volatile components, e. g. N-methylpyrrolidine **(4)**, N-methyl-Δ³-pyrroline **(5)**, and/or N-methylpyrrole **(6)**. For separation and identification of **4–6** we developed a GC-MS-procedure (Fig. 2). **4, 5**, and **6** proved to be stable under the pertinent conditions provided there is no Pd present (see below).

GC-MS-analysis of the volatile components from the dehydrogenation of **1** (Scheme) indicated that a N-methyl-

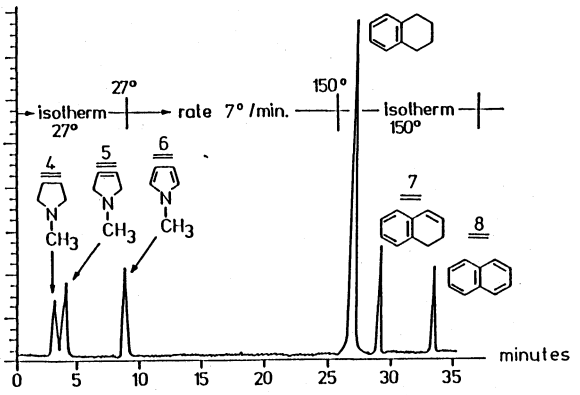


Fig. 2: GC–MS–Separation

pyrroline ($M^{+\cdot}$ = m/z 83) and traces of **4** ($M^{+\cdot}$ = m/z 85) had been formed. The quantity of the N-methylpyrroline was too small for ^{1}H-NMR spectroscopy. In the GC-EI-MS of this compound no loss of $\cdot C_2H_3$ (27 mu) from $(M-1)^+$ was observed nor did we find the elimination of $H_2C=CH_2$ from $M^{+\cdot}$ which is reported for molecules containing a Δ¹-pyrroline increment[4]. So we assumed that N-methyl-Δ³-pyrroline **(5)** had been generated. For its identification we needed authentic **5**.

Various methods for the preparation of **5** are reported: *Lukeš* et al.[5] reduced **6** with Zn/HCl to a mixture of **5** and **4**, which – as we found – contains components with $M^{+\cdot}$ > m/z 85. This mixture was separated by prep. GC. – *Tsuchiya*[6] reduced **6** according to *Knorr*[7], but contrary to his finding a mixture of about 68 % **5** and 32 % **4** arose in our hands (^{1}H-NMR spectroscopy). – *Lehn* et al.[8] synthesized N-methyl-Δ³-pyrroline for NMR-experiments without giving experimental details, condensing cis-1,4-dichloro-2-butene with methylamine using *Bobbitt*'s general approach[9] for N-alkylated Δ³-pyrrolines.

After various trials this twofold condensation yielded 60–80 % **5** in our hands (cf. Exp. Part). **5** is extremely volatile, it is identical with the N-methylpyrroline obtained in the dehydrogenation of **1** (GC, MS).

In order to find out whether **5** is stable under the conditions used for the dehydrogenation of **1** to **2** and **3**, we treated **5** with Pd/C in tetralin at 190 °C and found some **6** besides the educt **5**. Tetralin had been dehydrogenated to 1,2-dihydronaphthalene **(7)** and naphthalene **(8)** (GC). On the other hand parts of **6** were hydrogenated to **4** and **5**.

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Experimental Part

N-Methyl-Δ^3-pyrroline **(5)**

To 5.1 g (41 mmol) of cis-1,4-dichloro-2-butene cooled to 0 °C in an autoklave were added 3.9 g (42 mmol) methylamine (33 % in absol. ethanol), previously cooled to −5 °C. The mixture was cooled to −50 °C, then the autoklave was closed and pressurized to 17 bar by N_2. Under stirring for 3 h the mixture was allowed to warm up to room temp. Before opening the autoklave was cooled to −78 °C, then the mixture was acidified with conc. HCl and evaporated to dryness. The crystals were washed with absol. diethylether, dried i. vac. and transfered to a 2-necked flask equipped with a *Vigreux* column. Dropwise addition of 60 % KOH liberated **5** which was fractionated at 75–81 °C. The receiving flask had been cooled to −78 °C, because **5** is very volatile: 2.73 g **5** (80 %). – ^{1}H-NMR (250 MHz): δ (ppm) = 2.47 (s; 3H, N-CH_3), 3.45 (s; 4H, 2 CH_2), 5.74 (s; 2H, 2 CH). – MS: m/z = 83 ($M^{+\cdot}$, 54 %), 82 (100), 81 (14), 80 (18; 82 − H_2, *78.05), 67 (29; 82 − $^{\cdot}CH_3$, *54.74), 55 (20).

Preparative separation of **5** *and* **4** *by GC*

A mixture of products obtained by reduction according to *Lukes*[5] containing **5** and 21 % **4** was separated by prep. GC: Column 3 m, 3/8″, 18 % ODPN on 60/80 mesh Chromosorb P/DMCS, desactivated by treatment with KOH; flow: 200 ml H_2/min, 20 °C; detector: TCD, 110 °C.

Dehydrogenation of **1**

220 mg (0.54 mmol) 3,4-dihydromacrostomine **(1)** and 70 mg Pd/C (10 %) in 3 ml of tetralin (freshly distilled over a 1 m-*Vigreux* column) were transfered to a 2-necked flask (Fig. 1) and heated under a smooth stream of N_2 for 2 h at 190 °C. Volatile components were trapped in tetralin cooled to −30 °C. These tetralin phases were examined by GC-MS. N-Methyl-Δ^3-pyrroline **(5)** and traces of N-methylpyrrolidine **(4)** were found.

Treatment of **5** *and* **6**, *respectively, with Pd in tetralin*

200 mg of N-methyl-Δ^3-pyrroline **(5)** and 100 mg Pd/C (10 %) in 1 ml freshly distilled tetralin were heated at 190 °C for 3 h. After cooling the mixture was examined by GC-MS. – Results: $M_1^{+\cdot}$ at m/z 83 **(5)** and $M_2^{+\cdot}$ at m/z 85 **(4)**. Besides tetralin compounds **7** and **8** were identified by GC (Fig. 2).

The same experiment was performed with 200 mg of N-methylpyrrole **(6)**: $M_1^{+\cdot}$ at m/z 81 **(6)**; $M_2^{+\cdot}$ at m/z 83 **(5)**; $M^{3+\cdot}$ at m/z 85 **(4)**. Again we found **7** besides **8** (GC).

GC-MS-Conditions

GC: Varian 3700; column: Glas capillary OV 225; 50 m; 0.25 mm diameter. – *GC-MS*: open coupling; injection: 0.07 µl; injection temp.: 200 °C; split: 2 ml/min; flow: 0.7 ml/min; carrier gas: He.

Mass spectrometer: Varian MAT 112 S, equipped with a computer SS 200; EI/CI ion source; electon energy: 70 eV; source temp.: 200 °C.

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[Ph 430]