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Yanhe Huang [a] & Rolf W. Hartmann [a]
[a] Fachrichtung 12.1 Pharmazeutische Chemie, Universität des Saarlandes, P.O. Box 15 11 50, D-66041, Saarbrücken, Germany

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THE IMPROVED PREPARATION OF 7,8-DIHYDRO-QUINOLINE-5(6*H*)-ONE AND 6,7-DIHYDRO-5*H*-1-PYRINDIN-5-ONE

Yanhe Huang[a] and Rolf W. Hartmann*

Fachrichtung 12.1 Pharmazeutische Chemie, Universität des Saarlandes, P.O. Box 15 11 50, D-66041, Saarbrücken, Germany

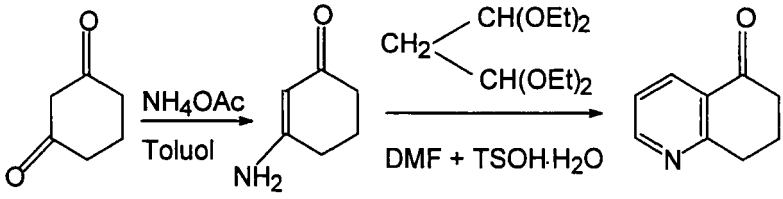
Abstract: Compounds 7,8-dihydroquinoline-5(6*H*)-one (**3**) and 6,7-dihydro-5*H*-1-pyrindin-5-one (**5**) are formed by new methods from 1,3-diketone compound, ammonium acetate and 1,1,3,3-tetraethoxylpropane.

The compounds **3** and **5** are versatile intermediates in organic synthesis and medicinal chemistry. Usually, these two compounds are prepared from propiolaldehyde and the corresponding enaminone [1,2,3] . Propiolaldehyde is unstable and difficult in preparation[4,5]. Enaminones are produced by reaction[3,6] of 1,3-diketones with gaseous ammonia which is of difficulty in manipulation.

This paper introduces new methods for preparation of **3** and **5**. Intermediate 3-aminocyclohex-2-enone **2** is produced by the reaction

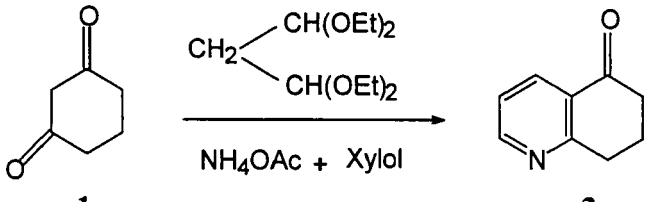
* To whom correspondence should be addressed.
a. Present address: Organic Pharmaceutical Chemistry, Uppsala University, BMC, S-75123, Uppsala, Sweden.

of 1,3-cyclohexanedione **1** with ammonium acetate instead of gaseous ammonia under toluol azeotropic removal of water. The reaction is very simple to operate and its yield very high. Compound **3** is produced by the reaction of **2** with commercially available 1,1,3,3-tetraethoxylpropane in place of propiolaldehyde.

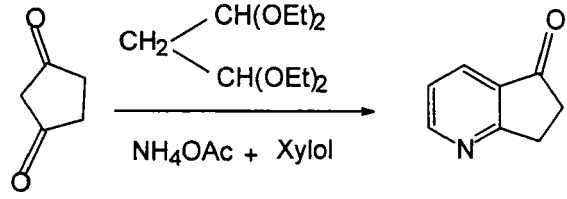


1 **2** **3**

Subsequently the two synthetic steps could be successfully combined. In an one pot synthesis all reactants and solvent are added to reaction vessel and heated under reflux, before the mixture is distilled in vacuo to give the product **3** and **5**.



1 **3**



4 **5**

Experimental

All reactions are carried out under nitrogen atmosphere. Benzene, toluol and xylol are distilled from sodium, DMF is dried with magnesium sulfate and distilled under reduced pressure. All solvents are stored over 4A° molecular sieves. Melting points are determined on a kofler microscope (Reichert, Vienna) and uncorrected. ^{1}H-NMR spectra are measured on a Bruker AW 80 (80MHz) and chemical shifts are reported in ppm downfield from TMS.

3-Aminocyclohex-2-enone (2). To a mixture of 3.85g (50mmol) of ammonium acetate in 100ml dry toluol is added 50mmol of **1**, then the mixture is stirred and heated under reflux with a Dean-Stark water separator for 5h. After replacing distillation apparatus, the reaction mixture is distilled at reduced pressure. The remaining crude mixture is recrystallized with ethyl acetate to give a yellow-crystalline material **2**, 5.06g (yield 91%), m.p. 133-134°C (lit[1],y. 50%, m.p.128-131°C). ^{1}H-NMR (DMSO-d_6) : 1.65-2.40(m, 6H), 4.94(s, 1H), 6.68(br.s. 2H).

7,8-dihydroquinoline-5(6*H*)-one (3). (A). A solution of 12ml (50mmol) of 1,1,3,3-tetraethoxylpropane, 5.55g (50mmol) of **2** and a catalytic amount of *p*-toluenesulfonic acid hydrate in 20ml DMF is heated under reflux for 18h. The solution is evaporated under reduced pressure, then the residual oil is distilled in vacuo (b.p. 40-46°C, 0.015-0.03mmHg) to give the target compound **3** as a colorless oil, 2.8g (Yield 38%) (lit.[1] total y. 29%). ^{1}H-NMR ($CDCl_3$): 2.05-2.40 (m, 2H, 7-H), 2.68 (t, J=6.6Hz, 2H,8-H), 3.15(t, J=6.2Hz, 2H, 6-H), 7.30 (dd, J=4.9 and 7.9Hz, 1H, 3-H), 8.30 (dd, J=1.8 and 7.9Hz, 1H, 4-H), 8.70 (dd, J=1.8 and 4.9Hz, 1H, 2-H).

(B). A suspension of 3.85g (50mmol) of ammonium acetate, 50mmol of **1** and 12ml (50mmol) of 1,1,3,3-tetraethoxylpropane in 40ml dry xylol is heated under reflux for 16h while the water and alcohol formed are removed azeotropically using a Dean-Stark apparatus.

The reaction mixture is concentrated at reduced pressure, then the residual oil is distilled in vacuo (b.p.40-46°C,0.015-0.03mmHg) to give the target compound **3** as a colorless oil, 2.5g (yield 34%).

6,7-dihydro-5*H*-1-pyrindin-5-one (5). The procedure of aforesaid method (B) is followed. The mixture of 25mmol of ammonium acetate, 25mmol of **4** and 6ml (25mmol) of 1,1,3,3-tetraethoxylpropane in 20ml dry xylol is reacted for 16h to produce compound **5** as a black solid (b.p.45-50°C, 0.02-0.03mmHg, lit.[3] b.p. 130°C, 12mmHg), which is recrystallized with benzene to give brown solid 0.82g (y. 26%) , m.p. 58-59°C (lit. [3] total y. 22%, m.p. 57-59°C). ^{1}H-NMR ($CDCl_3$): 2.60-2.85 (m, 2H,7-H), 3.10-3.40 (M, 2H, 6-H9, 7.30 (dd, J=6.0, 8.8 Hz, 1H, 3-H), 8.0 (dd, J= 1.8, 8.8 Hz, 1H, 4-H), 8.90 (dd, J=1.8, 6.0Hz, 1H, 2-H).

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