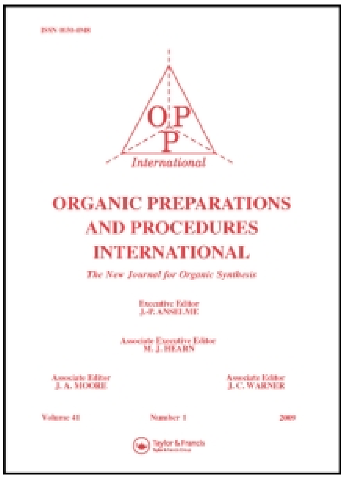

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AN IMPROVED METHOD FOR THE PREPARATION OF 5-HYDROXY-2-PYRROLIDONE

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AN IMPROVED METHOD FOR THE PREPARATION OF 5-HYDROXY-2-PYRROLIDONE

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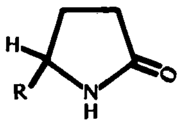
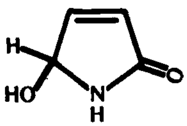
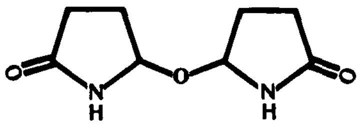
In connection with another study, we needed an efficient method for preparing large quantities of 5-hydroxy-2-pyrrolidone (**Ia**), previously obtained by the photooxidation of a dilute (0.1%) aqueous solution of pyrrole to produce a 32% yield of 5-hydroxy-Δ^3-pyrrolin-2-one (**II**),[1,2] which was hydrogenated to **Ia**.[1] Although the need to run the photooxidation step in dilute solution limits the amount of **Ia** which could be prepared, a more severe problem is the formation of significant amounts of 2-pyrrolidone as a side-product during the reduction of **II** to **Ia**.[3]



I



II



III

a) R = OH b) R = OEt

We reasoned that succinimide might be a suitable precursor to **Ia** if one carbonyl group could be selectively reduced. Recently, Speckamp and coworkers[4] demonstrated that N-substituted succinimides are reduced with sodium borohydride in ethanol to afford N-substituted-5-ethoxy-2-pyrrolidones or N-substituted-5-hydroxy-2-pyrrolidones, depending on the method of isolation. Furthermore, they converted succinimide to 5-ethoxy-2-pyrrolidone (**Ib**) in high yield; however, only polymeric material was obtained in an attempt to obtain **Ia** from succinimide by direct reduction.[5]

The reported procedure,[4] gave us a 90% yield of 5-ethoxy-2-pyrrolidone (**Ib**) from succinimide; an aqueous solution of **Ib** in the presence of a drop of conc. HCl decomposed to a polymeric oil within a few minutes. We found that refluxing an aqueous solution of **Ib** for 8 hrs. afforded **Ia** in 85% yield. In addition to unreacted **Ib**, workup of a hydrolysis interrupted after 1 hr. gave a different product, characterized as **III** on the basis of its spectral properties. Several hours reflux of **III** in water resulted in a quantitative conversion to **Ia**.

EXPERIMENTAL

*5-Hydroxy-2-pyrrolidone (***Ia***)* — A solution of 5-ethoxy-2-pyrrolidone[4] (2.05 g, 0.016 mol) in distilled water (25 ml) was heated at reflux for 8 hr, cooled and evaporated *in vacuo*. The semisolid residue was triturated with ethyl acetate, filtered and recrystallized from acetone to afford **Ia** (1.35 g, 85%), mp. 98-101°, lit.[1] mp. 98-99°; ^{1}H nmr (DMSO-d$_6$): 8.13 (br s, 1H, NH, exchanges with D$_2$O), 5.67 (d, 1H, OH, exchanges with D$_2$O), 5.10 (m, 1H, H-5), and 2.30-1.50 (m, 4H, CH$_2$CH$_2$); ^{13}C nmr: (D$_2$O) 181.3 ppm (C = O), 79.8 ppm (CH-OH), 29.4 and 28.5 ppm (CH$_2$CH$_2$); mass spec (70 eV): m/e 101 (M$^+$, base peak), 84 (M-OH), 83 (M-H$_2$O); high resolution mass spec: m/e 101.0489; IR (KBr): 3.15, 6.05, 6.15, 6.80, 7.10, 7.60, 7.95, 8.65, 9.15, 9.40, 9.90 and 11.50 cm^{-1}.

Anal. Calcd for C$_4$H$_7$NO$_2$: C, 47.52; H, 6.98; N, 13.86. Found: C, 47.38; H, 6.66; N, 13.51.

*2,2'-Oxo-5,5'-bispyrrolidinyl ether (***III***)* — A solution of 5-ethoxy-2-pyrrolidone (5.0 g, 0.039 mol) in water (200 ml) was refluxed for 1 hr, cooled and the solvent was removed *in vacuo*. The semisolid residue was triturated with ethyl acetate and filtered to give **III** (2.1 g, 54%), mp. 154-156°C; IR (KBr): 3.00, 3.20, 5.95, 7.85, 9.65 and 10.15 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): δ 8.55 (br s, 1H, NH, exchanges with D$_2$O), 5.07 (m, 1H, H-5) and 1.70-2.40 (m, 4H, -CH$_2$CH$_2$-); ^{13}C nmr (D$_2$O) 181.92 ppm (C = O), 85.07 ppm (CHOR), 28.42 and 28.22 ppm (-CH$_2$CH$_2$-); mass spec (70 eV) m/e 101, 85, 84 and 83 no molecular ion observed.

Anal. Calcd for C$_8$H$_{12}$N$_2$O$_3$: C, 52.16; H, 6.57; N, 15.21. Found: C, 52.10; H, 6.54; N, 15.15.

Evaporation of the filtrate *in vacuo* afforded 5-ethoxy-2-pyrrolidone (2.0 g, 40%), mp. 48-52°, lit.[4] mp. 48-52°, after recrystallization from ether.

Conversion of **III** *to* **Ia** — A solution of **III** (1.70 g, 0.009 mol) in water (100 ml) was heated at reflux for 12 hr, cooled, the solvent was removed *in vacuo* and the residue recrystallized from acetone to afford pure **Ia** (1.60 g, 90%), mp. 98-101°, lit.[1] mp. 98-99°.

REFERENCES

1. P. de Mayo and S.T. Reid, *Chem. and Ind.*, 1576 (1962).
2. G.B. Quistad and D.A. Lightner, *Chem. Commun.*, 1099 (1971).
3. In some cases 2-pyrrolidone was the major product in the reduction of **II** and probably arises from overreduction of **Ia** due to the activity of our catalyst. By monitoring the course of the reduction by tlc we observed that 2-pyrrolidone was formed at the expense of **Ia**. The rate of the reduction of **Ia** to 2-pyrrolidone must be comparable to the rate of reduction of **II** to **Ia** since the presence of **II** was detected throughout the course of the reduction.
4. J.C. Hubert, J.B.P.A. Wijnberg and W.N. Speckamp, *Tetrahedron*, **31**, 1437 (1975).
5. Private communication to B.W.C. from Professor Speckamp.

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