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# ONE-STEP SYNTHESIS AND STRUCTURAL CONFIRMATION OF 1-PYRROLINE TRIMER

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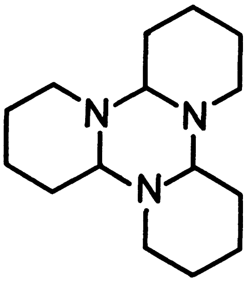
Oxidation of pyrrolidine with aqueous alkaline solution of sodium peroxodisulfate in the presence of silver nitrate gave 1-pyrroline trimer in moderate yield with remarkable selectivity and its structure was established.

While pure 2,3,4,5-tetrahydropyridine trimer (1) has been prepared by a variety of procedures[1a)] and its structure has recently been thoroughly studied,[1b)] the preparation and the structure of its homolog, 1-pyrroline trimer (2), have still been ambiguous due to its thermal and acid lability. Although the liquid supposed to be 1-pyrroline trimer was obtained by Fuhlhage and Van der Werf,[2)] it was never isolated in the pure form and its physical properties were not characterized.

In the present communication we wish to report the first one-step synthesis of 2 by the silver-catalyzed oxidation of pyrrolidine with peroxodisulfate and its complete structural analysis.



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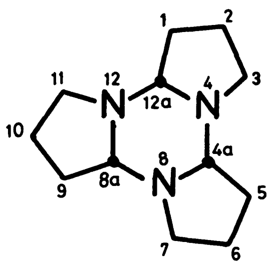

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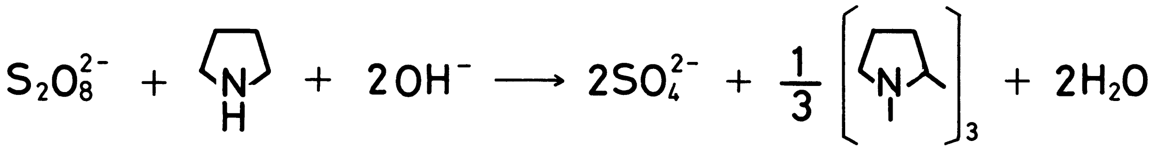
It was previously reported by Bacon et al.[3)] that treatment of aliphatic amines with aqueous alkaline solution of sodium peroxodisulfate in the presence of silver nitrate gave aldehydes or ketones via imine intermediates, the yield being low and variable in the case of secondary amines. In the present investigation a similar reaction using secondary cyclic amines was carried out in connection with our interest in the reactivity of cyclic imines. Unlike the procedure of Bacon and coworkers, however, in the present oxidation procedure one mole excess of sodium hydroxide was used; a 25 % aqueous solution of sodium peroxodisulfate $Na_2S_2O_8$ (150 mmol) was added dropwise at 0 °C to a stirred mixture of pyrrolidine (150 mmol), sodium hydroxide (300 mmol) and a catalytic amount (0.75 mmol) of silver nitrate in water (150 ml) and the mixture was stirred for additional 2.5 hr. The usual work-up of the reaction mixture with dichloromethane gave almost pure 2 in 50 % yield as a faint orange oil, which was found to be of satisfactory purity for nmr spectra. Due to its facile decomposition even at 40 °C and acid sensitivity,[4] further purification was of special difficulty.[2] After several experiments it was found that the analytically pure 2 could be obtained as a colorless oil by eluting the product through the neutral alumina column with ether; Found: C, 69.22 ; H, 10.51 ; N, 20.06 %. Calcd for $C_{12}H_{21}N_3$: C, 69.52 ; H, 10.21 ; N, 20.27 %.

The reaction may be shown by the following equation.



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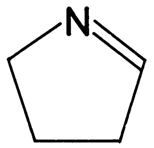
To the best of our knowledge, the molecular weight of 2 has not been established irrespective of its having been called "a trimer of 1-pyrroline".[2] A mass spectroscopic analysis suggested that 2 readily decomposes under the measurement conditions into the corresponding monomer 1-pyrroline (3). Cryoscopic measurement of a benzene solution, however, revealed that the molecular weight of 2 is 207 ± 22. It can therefore be concluded without ambiguity that it is a trimeric species of 3. The structure of the trimer was most explicitly suggested by its $^{13}$C-nmr spectrum (20 MHz), which indicated four peaks at $\delta_{TMS}$(in $CDCl_3$) 81.96 (C-4a, C-8a, C-12a), 45.79 (C-3, C-7, C-11), 27.96 (C-1, C-5, C-9), and 20.37 (C-2, C-6, C-10) in complete agreement with its apparent $C_3$ symmetry.[5] $^1$H-off-resonance decoupled $^{13}$C-nmr spectrum cleary showed three triplets and a doublet in accord with the presence of nine methylene and three methyne carbons in the molecule with $C_3$ symmetry. Assignment of signals in the $^{13}$C-nmr spectrum rests on comparison of the chemical shifts with the calculated values based on the additivity of chemical shifts.[6] The presence of proton attached to the $sp^2$ carbon atom was precluded by its $^1$H-nmr spectrum which showed complex multiplets at $\delta_{TMS}$(in $CDCl_3$)



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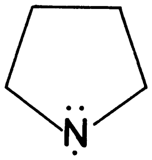
3.1 (6H), 2.4 (3H), and 1.9 (12H). Thus the structure of the trimer can most reasonably be represented by 2.

It should be emphasized that the simple preparative procedure empolyed here gave 2 with remarkable selectivity. Several trials to prepare 1-pyrroline have been reported; i) hydrolysis of 4-aminobutanal diethyl acetal,7) ii) catalytic partial dehydrogenation of pyrrolidine,2) iii) catalytic hydrogenation of pyrrole,2) iv) dehydrohalogenation of 1-chloropyrrolidine2) and v) periodate degradation of 3-hydroxypiperidine.2) However, 1-pyrroline was only trapped as the condensation product with *o*-aminobenzaldehyde or pyrrole, and 1-pyrroline trimer, which must have existed in the reaction system, was never isolated in the pure form.

It should also be noted here that the present reaction is most likely to proceed via a radical process involving 1-pyrrolidinyl radical 4 rather than via a heterolytic process involving 1-pyrrolidinylium ion 5 which might be produced by hydride abstraction.8) Further mechanistic studies are now in progress.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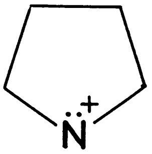
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## References and Notes

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4) The trimer decomposes upon silica gel column chromatography, TLC, GC and distillation in vacuo.
5) If the nitrogen inversion is faster than the time scale of nmr, 2 satisfies apparent $C_3$ symmetry regardless of its conformations, since all three methyne protons are supposed to be axial (unpublished results).

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