HETEROCYCLES, Vol 22, No 4, 1984

REDUCTION OF THE HERBICIDE DIQUAT WITH SODIUM BOROHYDRIDE-NICKEL (II) CHLORIDE: STRUCTURE OF THE TWO ISOMERIC PERHYDRO-8a,10a-DIAZAPHENANTHRENES

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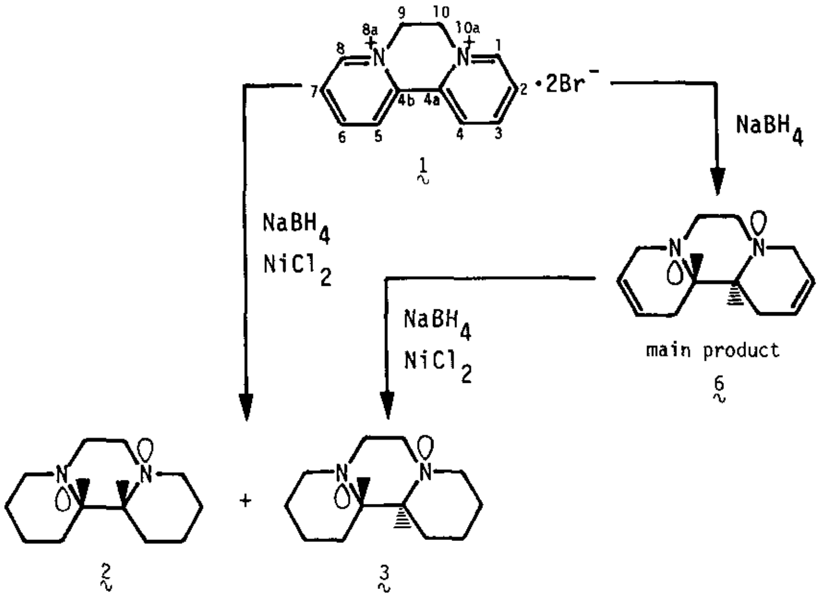
Abstract ——— The stereochemistry of isomeric perhydro-8a,10a-diazaphenanthrenes(2 and 3) obtained by sodium borohydride-nickel (II) chloride reduction of the herbicide, diquat (1), was confirmed by X-ray crystallographic analysis of the hydrobromide of 2, and of the hydrochloride of partially reduced product, 1,4,4a,4b,5,8,9,10-octahydro-8a,10a-diazaphenanthrene(6), which is converted with ease to 3.

In previous paper[1,2], we reported that diquat[9,10-dihydro-8a,10a-diazaphenanthrene dibromide(1)], effective contact herbicide, in blood and urine of accidental and suicidal poisonings can be conveniently determined by gas-liquid chromatography(GLC) of its perhydrogenated products obtained by reduction with sodium borohydride($NaBH_4$) in the presence of nickel(II) chloride($NiCl_2$). On GLC, the reduction products of 1 emerged as two peaks in the integral ratio of 1.0:0.36 for 3 and 2, but the ratio was significantly different from that(0.42:1.0 for 3 and 2) of catalytic hydrogenation[3,4] with platinum dioxide of 1. This fact suggests that the mechanism for the $NaBH_4$-$NiCl_2$ reduction of 1 differs from that for the catalytic hydrogenation. The stereochemistry of the perhydrogenated products(2 and 3), however, has not been established to date.

In this communication, we wish to report the determination of cis and trans configuration of both hydrogen atoms at C-4a and C-4b in two isomeric perhydro-8a,10a-diazaphenanthrenes(2 and 3) obtained by the reduction of 1.

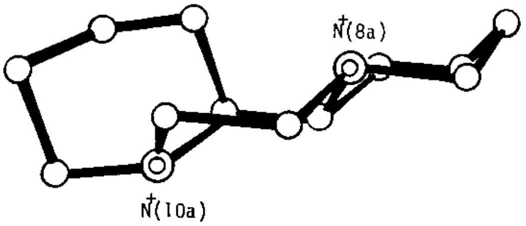


Scheme 1

Reduction of 1(1 mM) with NaBH$_4$(10 mM) in the presence of NiCl$_2$(2 mM) in methanol or water gave a mixture of perhydrogenated products(2 and 3) in 92% yield as a colorless oil(bp *100-102°C/6mmHg*). *The reduction preceeds under the continuous* evolution of hydrogen along with the formation of black nickel boride. Thin-layer chromatography(alumina; solvent Et$_2$O) of the reaction mixture allowed isolation of 2 and 3. The reduction products(2 and 3), however, were unstable upon exposure to air. Consequently, separation of the reduction products was achieved by fractional crystallization of the corresponding hydrobromides(4 and 5) from methanol.[4, rhombuses, mp 290°C<(dec.), 5, needles, mp 310°C<(dec.)]

Mass spectra of both free bases(2 and 3) showed a similar fragmentation pattern (*main fragment m/z:* 194, 111, 98, 83). Ir spectra of 2 and 3(1.5% CHCl$_3$ solution) showed Bohlman bands[5] at 2760 and 2810 cm^{-1}, respectively. The intensity of the bands of 3, however, was two times stronger than that of 2. Satisfactory information of their stereochemistry was also not obtained on the basis of the ^{1}H-nmr spectra of 2 and 3.

Thus, we carried out X-ray crystallographic analysis of the hydrobromides(4 and 5). Intensity data were collected in a Syntex R3 four-circle diffractometer with the graphite-monochromated Mo Kα radiation using the ω-scan mode. Crystal data for 4: $C_{12}H_{22}N_2\cdot 2HBr$, monoclinic, space group P2$_1$/c, a=13.790(8), b=8.591(5), c=12.218 (9) Å, β=101.42(5)°, z=4, Dx=1.68 g/cm^3, and μ(Mo Kα)=60.3 cm^{-1}. A total of 1937 independent reflections was collected with in 2θ less than 45°. The structure of 2 was solved by the heavy atom method, and refined by a block-diagonal least-squares method to the R-value of 0.080(for 1325 reflections) excluding all the hydrogen atom. By interpretation of high peaks on Patterson function, the coordinates of the bromine atoms were easily determined.



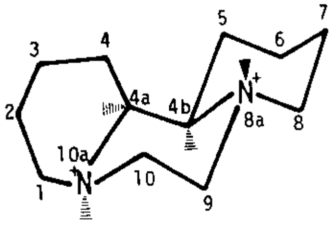


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Fig. 1 Perspective view of the molecule of 4

The X-ray crystallographic analysis of 4 clearly indicates that the configuration of both hydrogen atoms at C-4a and C-4b of 4 adopts a cis-orientation(see Fig. 1). Unfortunately, X-ray crystallographic analysis of the hydrobromide(5) was unsuccesful because deformation of its crystalline form by the X-ray irradiation. Our previous work has demonstrated that the reduction of 1 with $NaBH_4$ in water results in the formation of several reduction products^6. The structure of a main reduction product was assigned to the partially reduced octahydro-8a,10a-diazaphenanthrene(6)^6. The reduction of the partially reduced product(6) with $NaBH_4$-$NiCl_2$ gave easily fully reduced product(3). Thus, the hydrochloride(7)^7 was subjected to the X-ray crystallographic analysis.

Crystal data for 7: $C_{12}H_{18}N_2 \cdot 2HCl \cdot 2H_2O$, monoclinic, space group $P2_1/c$, a=18.929(13), b=7.449(4), c=20.124(13) Å, β=102.02(5)°, z=8, Dx=1.42 g/cm^3, and μ(Mo Kα)=4.7 cm^{-1}. A total of 2582 independent reflections was collected with 2θ less than 40°. The structure was solved by a direct method using the MULTAN program^8 and refined by a block-diagonal least-squares method to the R-value of 0.071(for 2353 reflections) excluding all the hydrogen atom except two hydrogen atoms bonded the oxygen atom of the one water molecule. The bond distances, angles and the conformations of two independent molecules in 7 are similar to each other.

The molecular structures of 7 are illustrated in Figure 2. The result evidently indicates that the hydrogen atoms at C-4a and C-4b of 7 adopt a trans-orientation. The position of two double bonds of 6 was also determined to be Δ^2 and Δ^6.

On the basis of the X-ray crystallographic results of **4** and **7**, it can be concluded that the reduction products(**2** and **3**) adopt the *cis* and *trans* configurations at C-4a and C-4b, respectively. The present result may shed some light on the elucidation of the mechanism of the $NaBH_4$-$NiCl_2$ reduction.

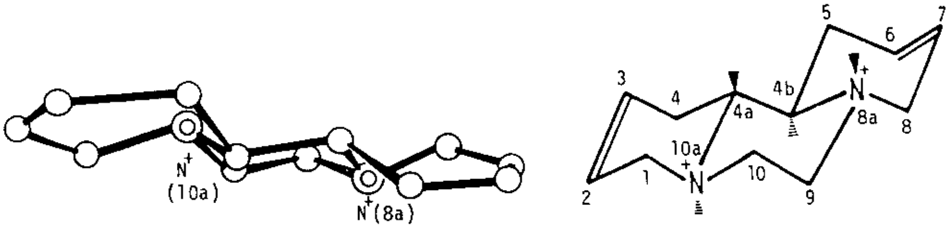

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Fig. 2 Perspective view of the molecule of **7**[9]

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7. The products obtained by the reduction of **1** with $NaBH_4$ were treated with hydrochloric acid. The mixture of the hydrochlorides thus obtained was separated to give a pure salt(**7**) as colorless pillars[mp 250°C<(dec.)] by fractional crystallization from methanol.
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9. One of the two independent molecules in a unit cell is described.

Received, 12th December, 1983