SYNTHESIS AND STRUCTURE OF 6,7-DEHYDROGLAUCINE

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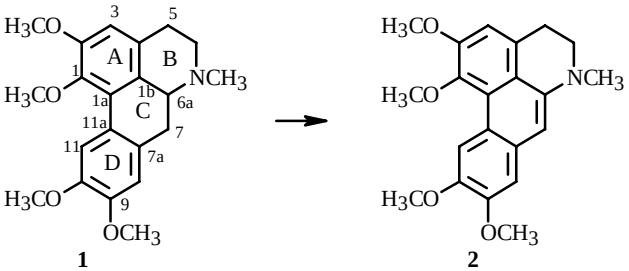
The syntheses of several aporphine alkaloids and their derivatives have been reported [1-3]. In continuation of this research, we studied the dehydrogenation of glaucine by mercury acetate.

In initiating the investigation of glaucine oxidation, we utilized the tendency of cyclic tertiary amines to dehydrogenate and form a C=C double bond in the α,β-position to the N atom [4] and the possibility that the dehydrogenation in polycyclic glaucine would occur in several competing directions, the priority of which was difficult to predict a priori.

Investigations showed that mercury acetate in the presence of $NaBH_4$ dehydrogenates glaucine regioselectively to form 6,7-dehydroglaucine (**2**).



1 **2**

The regioselective dehydrogenation of glaucine at the 6 and 7 positions of ring C and not at the 4 and 5 positions of ring B is apparently due to the lower strength of the C–H bonds in these positions and the driving force for the molecule to form the more energetically favorable and stable conjugated aromatic ring and not the acyclic conjugated system of ring B, which has less stabilization energy.

The structure of 6,7-dehydroglaucine was confirmed by IR, PMR, and ^{13}C NMR spectra and an x-ray structure analysis. Figure 1 shows the molecular structure of **2**.

The bond lengths and angles are close to the usual values [5] except for the C6=C7 double bond at 1.355 Å. Ring C1C2C3C5C14C13 is planar within ±0.0028 Å. The piperidine ring C4C5N1C6C14C15 adopts an almost ideal chair conformation ($\Delta C_s^5 = 1.46°$) with atom C5 deviating from the average plane of the remaining atoms by 0.64 Å, like in 7-hydroxyglaucine methiodide [6]. Ring C16C8C9C10C11C12 is planar within ±0.015 Å. All methoxyls lie in the plane of the aromatic rings except for the methoxyl on C1, which is twisted perpendicular to the plane of the ring (torsion angle C2C1O1C17 = 81.67°).

6,7-Dehydroglaucine (2). Glaucine (100 mg) was dissolved in $CHCl_3$ (20 mL) and treated with mercury acetate (0.012 mg) and $NaBH_4$ (0.009 mg). The reaction was carried out at room temperature for 3 h. The solution was filtered. The filtrate was washed with water and extracted three times with $CHCl_3$. The $CHCl_3$ exstract was dried over anhydrous Na_2SO_4. The solvent was evaporated. The solid was chromatographed over a column of Al_2O_3 (activity II) with elution by hexane to afford crystalline **2** in 45% yield, mp 120-123°C.

IR spectrum (KBr, ν, cm^{-1}): 1161, 1228 (OCH_3), 1540, 1613 (aromatic ring), 2824 ($N–CH_3$).

PMR spectrum (500 MHz, $CDCl_3$, δ, ppm, J/Hz): 2.99 (3H, s, $N–CH_3$), 3.02 (2H, t, J = 6, H-4), 3.27 (2H, t, J = 6, H-5), 3.85, 3.89, 3.90, 3.94 (3H, s, OCH_3), 6.61, 7.01, 7.20, 9.00 (1H, s, H-3, H-8, H-11, H-7).

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TABLE 1. Atomic Coordinates (Å×10^4; for H, Å×10^3) in Cell Fractions for **2**

Atom	x	y	z	Atom	x	y	z
O1	5990 (1)	5527 (2)	1846 (2)	H11	6495 (2)	4080 (2)	2890 (3)
O4	6838 (2)	1996 (2)	3807 (2)	H20A	9410 (2)	2020 (3)	6340 (3)
C9	7993 (2)	2975 (2)	5009 (3)	H20B	8633 (2)	2480 (3)	7310 (3)
O3	8152 (1)	1912 (2)	5556 (2)	H19A	9940 (2)	8680 (3)	6200 (3)
C7	8775 (2)	6019 (3)	5023 (3)	H7	9217 (2)	5900 (2)	5630 (3)
C11	7022 (2)	4058 (3)	3496 (3)	H20C	8770 (2)	1070 (3)	6960 (3)
C16	8253 (2)	5020 (2)	4672 (3)	H21A	6040 (2)	1140 (3)	2600 (3)
C14	7811 (2)	7209 (2)	3593 (3)	H21B	5680 (2)	2460 (3)	2800 (3)
N1	9069 (2)	8070 (2)	4905 (2)	H8	9000 (2)	3900 (2)	5860 (3)
C8	8475 (2)	3951 (2)	5284 (3)	H3	6788 (2)	9250 (3)	1810 (3)
C13	7283 (2)	6223 (2)	3190 (3)	H4A	8720 (2)	9410 (3)	2840 (3)
C12	7502 (2)	5097 (2)	3770 (3)	H19B	10160 (2)	7360 (3)	5950 (3)
C1	6567 (2)	6415 (3)	2246 (3)	H4B	7840 (2)	10000 (3)	3400 (3)
C10	7264 (2)	3026 (3)	4073 (3)	H19C	9310 (2)	7820 (3)	6820 (3)
C6	8564 (2)	7086 (2)	4547 (3)	H5A	8155 (2)	9150 (2)	5510 (3)
C15	7609 (2)	8305 (2)	3044 (3)	H21C	6510 (2)	2160 (3)	1880 (3)
C3	6909 (2)	8441 (3)	2116 (3)	H5B	9070 (2)	9770 (3)	5070 (3)
C4	8181 (3)	9329 (3)	3454 (4)	H17A	6060 (3)	5640 (4)	-40 (4)
O2	5675 (1)	7553 (2)	821 (2)	H18A	5270 (2)	9200 (3)	1160 (4)
C2	6389 (2)	7497 (3)	1717 (3)	H18B	5860 (3)	9030 (3)	-60 (4)
C20	8797 (2)	1868 (3)	6645 (3)	H17B	6790 (3)	4680 (3)	600 (4)
C21	6233 (3)	1932 (3)	2688 (4)	H17C	5660 (3)	4350 (4)	420 (4)
C19	9669 (3)	7968 (3)	6071 (3)	H18C	4810 (3)	8480 (3)	-150 (4)
C17	6173 (3)	5015 (4)	610 (4)				
C5	8596 (2)	9170 (3)	4819 (4)				
C18	5392 (3)	8664 (4)	361 (5)				

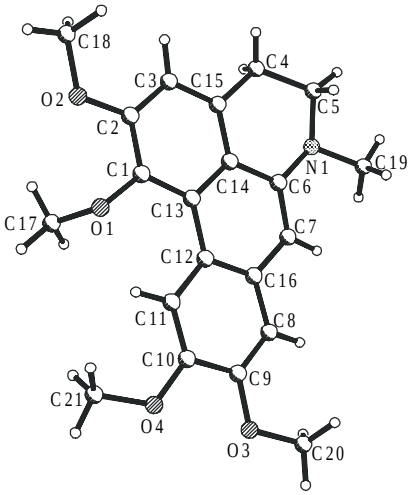

Fig. 1. Molecular structure of 6,7-dehydroglaucine.

^{13}C NMR spectrum ($CDCl_3$, 125.76 MHz, δ, ppm): 40.50 (N–$\underline{C}H_3$), 111.77 (C-4), 151.74 (C-5), 134.4 (C-6), 55.55 (1-OCH_3), 55.60 (2-OCH_3), 56.62 (10-OCH_3), 59.87 (9-OCH_3), 143.30 (C-3), 146.96 (C-2), 110.29 (C-1), 145.46 (C-9), 130.52 (C-11).

X-ray Structure Analysis. Unit-cell constants and intensities of 3817 independent reflections were measured on a Syntex $P2_1$ diffractometer (Cu Kα, graphite monochromatometer, θ/2θ-scanning, 2θ ≤ 140°). The crystals were monoclinic, a = 14.989(3), b = 11.549(2), c = 10.264(2) Å, β = 93.75(5)°, V = 1771.9(6) Å^3, d_{calc} = 1.325 g/cm^3, Z = 4 ($C_{21}H_{23}NO$), space group $P2_1/c$. The structure was solved by direct methods and refined by anisotropic full-matrix least-squares methods for

nonhydrogen atoms. H atoms were found in a difference synthesis and refined isotropically. A total of 3368 reflections with $I > 2\sigma(I)$ was used in the calculations. The final agreement factors were R = 0.057 and R_w = 0.1231. The structure was solved and refined using the programs SHELXS-97 and SHELXL-97. Table 1 lists the atomic coordinates.

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