

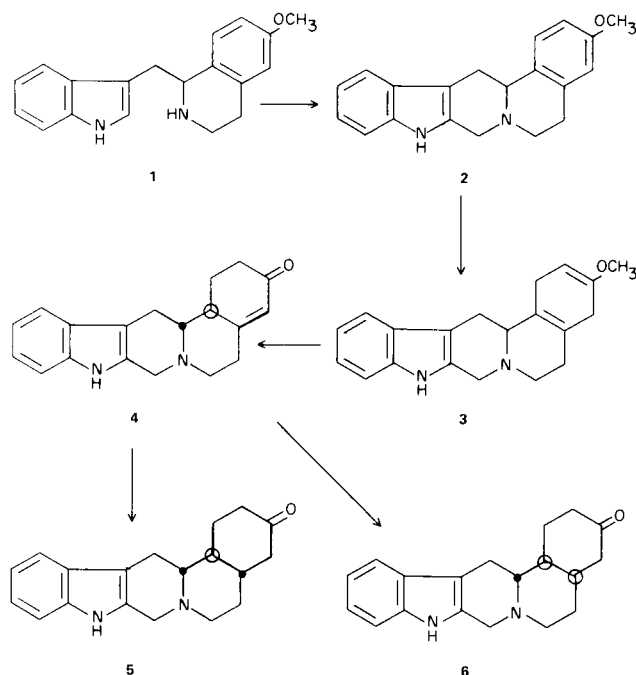
1,4,4a,5,6,8,9,14,14a,14b-Decahydrobenz[*a*]indolo[2,3-*g*]quinolizinones.
A System Isomeric with Yohimbane.

Glenn C. Morrison, Ronald O. Waite and John Shavel, Jr.

Department of Organic Chemistry, Warner-Lambert Research Institute,
Morris Plains, New Jersey 07950

Received May 14, 1971

Continuing with our interest in systems isomeric with the yohimbanes (1) we turned our attention to the benz[*a*]indolo[2,3-*g*]quinolizines. A member of this ring system in which ring 1 is aromatic has been described by V. Boekelheide (2). Utilizing their synthetic method we have cyclized the indolylmethyltetrahydroisoquinoline **1** to the monomethoxyhexahydrobenz[*a*]indolo[2,3-*g*]quinolizine **2**. Having the methoxy group as a handle we were able to reduce **2** to the octahydro derivative **3** via the Birch reduction. Hydrolysis of the enol ether function of **3** and conjugation of the double bond led to the α,β -unsaturated ketone **4**. The stereochemistry of **4** was assigned on the assumptions that the acid hydrolysis would afford the more thermodynamically stable form and that the anti form had the least steric interactions (3). Applying reduction procedures developed for the stereoselective reduction (4) of $\Delta^{1,8a}$ -2-decalone we reduced **4** with



sodium in liquid ammonia to *trans-anti*-1,4,4a,5,6,8,9,14,14a,14b-decahydrobenz[*a*]indolo[2,3-*g*]quinolizinone (**5**). The *cis-anti*-isomer (**6**) was obtained on catalytic reduction of **4**.

EXPERIMENTAL (5)

The melting points were determined using a Thomas-Hoover apparatus which had been calibrated against known standards. 5,6,8,9,14,14a-Hexahydro-3-methoxybenz[*a*]indolo[2,3-*g*]quinolizine (**2**).

To a solution of 29.2 g. of 1,2,3,4-tetrahydro-1-(indol-3-ylmethyl)-6-methoxyisoquinoline (**6**) and 3.96 ml. of 37% formaldehyde solution in 2 l. of 3% acetic acid was added 1 l. of a 1*N* sodium hydroxide solution over a 5 hour interval. Filtration of the reaction mixture gave a solid which after recrystallization from benzene afforded 22.0 g. (72%) of a solid m.p. 201.5-203.5°. Recrystallization from Skelly solve B gave an analytical sample m.p. 202-203.5°.

Anal. Calcd. for $C_{20}H_{20}N_2O$: C, 78.92; H, 6.62; N, 9.20. Found: C, 78.95; H, 6.60; N, 9.15.

1,4,5,6,8,9,14,14a-Octahydro-3-methoxybenz[*a*]indolo[2,3-*g*]quinolizine (**3**).

To a solution of 15.0 g. of 5,6,8,9,14,14a-hexahydro-3-methoxybenz[*a*]indolo[2,3-*g*]quinolizine in 500 ml. of tetrahydrofuran was added 1 l. of liquid ammonia. To the resulting solution was added 7.2 g. of sodium and 32 ml. of *t*-butyl alcohol in six equal portions over a 5 hour period. The unreacted sodium was destroyed with methanol and the ammonia was allowed to evaporate. The residue was poured into 1500 ml. of water. A solid was deposited which after slurring with 750 ml. of hot isopropyl ether gave 13.9 g. (92%) of a solid m.p. 212-214°.

Anal. Calcd. for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.38; H, 7.40; N, 9.16.

1,5,6,8,9,14,14a,14b-Octahydrobenz[*a*]indolo[2,3-*g*]quinolizin-3-(2*H*)one (**4**).

A solution of 10.2 g. of 1,4,5,6,8,9,14,14a-octahydro-3-methoxybenz[*a*]indolo[2,3-*g*]quinolizine and 75 ml. of hydrochloric acid in 200 ml. of methanol was refluxed for 1.5 hours. The methanol was removed *in vacuo* and 75 ml. of water was added. The solution was made basic with 40% sodium hydroxide solution and extracted with methylene chloride. The methylene chloride layer was washed with water, dried over sodium sulfate, and the solvent was removed. Trituration of the residue with

acetonitrile afforded 4.6 g. (48%) of a crystalline solid m.p. 217-224°. Further recrystallization gave an analytical sample m.p. 219-220°.

Anal. Calcd. for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.90; N, 9.58. Found: C, 77.82; H, 6.99; N, 9.41.

Trans-anti-1,4,4a,5,6,8,9,14,14a,14b-Decahydrobenz[a]indolo[2,3-g]quinolizin-3(2H)one (5).

To a solution of 3.0 g. of 1,5,6,8,9,14,14a,14b-octahydrobenz[a]indolo[2,3-g]quinolizin-3(2H)one in 125 ml. of tetrahydrofuran was added 250 ml. of ammonia. Then 0.12 g. of lithium was added and the mixture was stirred for 1 hour. The excess lithium was destroyed by the addition of 0.19 g. of ammonium chloride over a 1 hour interval and the ammonia was allowed to evaporate. On the addition of 700 ml. of water, there was deposited a solid which after recrystallization from benzene gave 1.8 g. (60%) of a crystalline solid m.p. 288-293°. Further recrystallization gave an analytical sample m.p. 300-304°.

Anal. Calcd. for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.25; H, 7.60; N, 9.67.

cis-anti-1,4,4a,5,6,8,9,14,14b-Decahydrobenz[a]indolo[2,3-g]quinolizin-3(2H)one (6).

To a solution of 1.0 g. of 1,5,6,8,9,14,14a,14b-octahydrobenz[a]indolo[2,3-g]quinolizin-3(2H)one and 6 ml. of 3*N* hydrochloric acid in 150 ml. of methanol was added 500 mg. of 10% palladium on charcoal and the mixture was hydrogenated. After hydrogen uptake had ceased the catalyst was removed by filtra-

tion. On concentration of the solution there was deposited a solid. The solid was shaken with 10% sodium hydroxide solution and methylene chloride. The methylene chloride layer was washed with water, dried over sodium sulfate, and the solvent was removed. Crystallization of the residue from ether afforded 0.33 g. (33%) of a crystalline solid m.p. 133-134°. Recrystallization from isopropyl ether gave an analytical sample m.p. 144-145°.

Anal. Calcd. for $C_{19}H_{22}N_2O$: C, 77.52; H, 7.53; N, 9.52. Found: C, 77.42; H, 7.57; N, 9.27.

REFERENCES

- (1) G. C. Morrison, W. A. Centenko and J. Shavel, Jr., *J. Org. Chem.*, **32**, 2768 (1967).
- (2) V. Boekelheide and C. Liu, *J. Am. Chem. Soc.*, **74**, 4920 (1952).
- (3) Based on an examination of two Dreiding models.
- (4) R. L. Augustine, *J. Org. Chem.*, **23**, 1853 (1958).
- (5) The authors are indebted to Mr. A. Lewis and his associates, to Dr. C. Greenough for the spectral data, and to Mrs. U. Zeek for analytical determinations.
- (6) G. C. Morrison, R. O. Waite and J. Shavel, Jr., *J. Org. Chem.*, **32**, 2555 (1967).