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Conformations and Base-catalyzed Equilibrations of N-Nitroso-decahydroquinolines and N-Nitroso-2-methyldecahydroquinolines

Short Communication

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Conformations of six title compounds were determined by ^{13}C-NMR spectroscopy. Equilibration of the 2-methyl-compounds gives as main products the derivatives of the amines least abundant in the product mixture of the catalytic hydrogenation.

(Keywords: $A_{1,3}$-strain; ^{13}C-NMR; Free energy differences)

Konformation und Base-katalysierte Äquilibrierungen von N-Nitroso-decahydrochinolinen und N-Nitroso-2-methyl-decahydrochinolinen (Kurze Mitt.)

Die Konformationen der sechs Titelverbindungen wurden mittels ^{13}C-NMR Spektroskopie bestimmt. Äquilibrierung der 2-Methyl-verbindungen ergab als Hauptprodukte die Derivate der bei katalytischer Hydrierung in geringster Menge entstandenen Amine.

Interest in the stereochemistry of decahydroquinolines initiated an investigation of the N-nitroso-derivatives of *trans*- and *cis*-decahydroquinolines: reaction with electrophiles after metallation[1,2], or base-catalyzed equilibration[2], followed by denitrosation might furnish substantial amounts of isomers formed only in very minor proportion by the catalytic hydrogenation or chemical reduction of the unsaturated compounds[3,4a].

N-Nitroso-*trans*-decahydroquinoline (**1**; mp. 32–33°; lit.[5] 32–33°), N-nitroso-*cis*-decahydroquinoline[4b] (**2**; mp. 7–9°), N-nitroso-2α-methyl-

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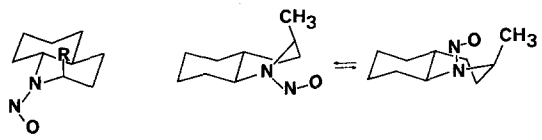
trans-decahydroquinoline* (**3**; mp. 85–86°), N-nitroso-2β-methyl-*trans*-decahydroquinoline* (**4**; mp. 29–30°), N-nitroso-2α-methyl-*cis*-decahydroquinoline* (**5**; mp. 19–20°) and N-nitroso-2β-methyl-*cis*-decahydroquinoline* (**6**) were prepared by reacting the respective amines[3,4a] with ethyl nitrite in anhydrous *THF*[1]. The conformational properties of **1**–**6** were determined by ^{13}C- and ^{1}H-NMR[4b,5] spectroscopy; conformer ratios were obtained by averaging integrations of > 5 pairs of corresponding signals.

Compounds **1** and **3** exist as single conformations with both rings in the chair form and the N—O *anti* to C-8a; the axial methyl group in **3** has no influence on the orientation of the nitroso group. At room temperature, two conformations in a ratio of 76:24 are observed for **4**; comparison of the ^{13}C shifts of both forms with **1** shows that the piperidine portion of the molecule must be twisted from the chair form (Scheme 1) due to the very high additional $A_{1,3}^{syn}$-strain caused by the equatorial methyl group. The similarity in the shifts of C-8a indicates that both conformations have the N—O bond *anti* to this carbon. If the probe temperature was raised to + 130°, all carbon atoms except C-2 and CH_3 showed single resonances, pointing to a rather low barrier of inversion between the two conformations.

Schema 1



1 : R = H
3 : R = CH_3

4

N-Nitroso-*cis*-decahydroquinoline (**2**) exists in the two conformations[4b] B-a and B-s shown in Scheme 2 ($R' = R'' = H$); the form with the N—O bond *anti* to C-8a (B-a) predominates slightly (ratio 55:45), No ring-inverted conformation A is seen because of the $A_{1,3}^{anti}$-interaction of the N—O group with C-8. Elevation of the probe temperature to + 130° has no palpable effect: the barrier of rotation around the N—N bond is much higher than the barrier of inversion for the two non-chair conformations of **4**. The two conformations B-a and B-s of **5** (Scheme 2, $R' = CH_3$, $R'' = H$) have the methyl group *syn*-axial to C-8 to avoid the

* Nomenclature: "β" means "substituent is on same ringside as substituent or hydrogen at C-4a"; "α" means "on opposite ringside". The new compounds **3**–**6** gave satisfactory elemental (C, H) analysis after distillation in a Kugelrohr (80°/0.05 Torr) and—for **3**–**5**—recrystallization.

Table 1. ^{13}C *Chemical Shifts of N-Nitroso-decahydroquinolines*[a]

Comp.	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-8a	C-4a	CH_3
1	40.4	24.9	31.8	32.5	25.4	25.4	28.9	66.9	44.0	—
3	42.7	29.4	26.9	32.5	25.5	25.5	29.2	62.0	43.6	15.4
4[b,c]	47.7	25.2	24.1	33.7	25.5	24.8	31.8	61.5	37.1	17.9
[d,c]	53.3	29.5	26.1	33.1	26.1	e	30.3	61.7	37.6	e
[f]	e	26.9	25.0	33.3	25.5	24.9	31.7	61.9	37.6	e
2[b]	35.5	24.9	24.3	30.4	20.6	25.0	26.2	60.9	36.3	—
[d]	46.7	26.4	24.6	30.8	20.3	25.3	23.0	49.4	34.6	—
5[b,g]	43.0	(30.3)	(20.6)	(31.1)	(20.4)	25.8	29.7	61.4	36.0	18.9
[d,g]	50.7	(30.5)	(20.6)	(31.1)	(20.8)	25.5	26.2	54.0	34.9	22.4
6[b,g]	53.8	35.3	(24.2)	30.7	20.2	(25.4)	(23.5)	50.1	34.7	19.1
[d,g]	43.9	(24.6)	(24.7)	25.9	25.9	20.8	27.8	56.1	37.0	15.7

[a] In ppm. Recorded on a Varian XL-100 Pulsed *Fourier* Transform Spectrometer, operating at 25.16 MHz, as 1 *M*-solutions in $CDCl_3$ + 4% Me_4Si, at + 30° unless indicated. [b] Major conformer. [c] Assignments ascertained by comparison with multideuterated analog (see ref.[3] for parent amine). [d] Minor conformer. [e] Not seen. [f] In *DMSO-d*$_6$, at + 130°. [g] Assignments which are not unambiguous are parenthesized.

sum of $A^{anti}_{1,3}$- and $A^{syn}_{1,3}$-strain of the nitroso group with C-8 and CH_3 in A; the conformation B-a is again predominant (ratio 57:43). Finally, the isomeric **6** (Scheme 2, $R' = H$, $R'' = CH_3$) exists in the conformations B-s and A in a ratio of 91:9. In both forms the nitroso group encounters an $A^{anti}_{1,3}$-strain with either CH_3 or C-8. In the parent amine the form with axial methyl is not observed[4a], which indicates a palpable reduction of the CH_3/C-4,8a interaction in the nitrosamine.

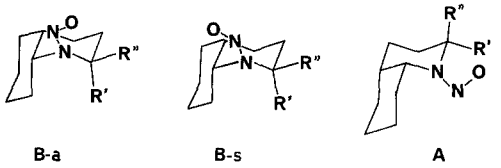
Equilibration reactions were carried out by stirring **1**-**6** with equimolar amounts of potassium-*t*-butoxide in *DMSO* at + 90° for 70 hours under N_2. The mixtures were diluted with water, made slightly acidic with CH_3CO_2H and extracted with petroleum ether. Material balance was ~ 90%. Equilibrium compositions were determined by glass capillary gas chromatography (SE 30; 40 m). Reproducibilities with various temperature programs was ± 0.2%; equilibrations starting with **1** or **2**, or with **3**-**6**, gave identical results (± 0.5%).

The equilibrium composition starting with **1** or **2** was 57% **1**, 43% **2**, corresponding to a ΔG° of 0.85 kJ/mol. Simple computation of stabilities by adding strain energies predicts a rather higher stability for **1** ($A^{anti}_{1,3}$ ~ 8.8 kJ/mol)[2] compared to **2** (C-8/C-2 + C-8/C-4 + C-6/C-4 ~ 11.9 kJ/mol), which is offset by an entropy term due to the two conformations of **2** ($\Delta G^\circ_{calc} = 3.1 - 2.1 = 1.0$ kJ/mol).

In the 2-methyl series the equilibrium composition starting with

either **3**, **4**, **5**, or **6** was 65% **3**, 2% **4**, 13% **5** and 20% **6**. This is again in good agreement with considerations based on strain energies: using values reported for N-nitroso-2-methyl-piperidines[2] (and neglecting the

Schema 2



2: $R' = R'' = H$
5: $R' = CH_3$, $R'' = H$
6: $R' = H$, $R'' = CH_3$

small amounts of the minor conformation of **6**), values of 16.7 (**3**), $\geq$25.9 (**4**), 24.1 (**5**) and 20.7 (**6**) kJ/mol are obtained. Correcting once more for the two conformations of **4** and **5**, only the result for **4** is low, which is not unexpected, since the piperidine ring in this case is not a chair, and the reported value[2] for the $A_{1,3}^{syn}$-strain was only a lower limit.

The equilibrium mixture of **3**–**6** contains as major components the two nitrosamines derived from the amines least abundant in the hydrogenation mixture of quinaldine[4a], which thus become available after denitrosation[1]. Since **3** crystallizes from the mixture, 2α-methyl-*trans*-decahydroquinoline can be easily obtained in pure form. A more detailed discussion with full spectral data and the results of a number of additionally substituted derivatives of **1**–**6** will be given in a full paper.

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