^{13}C NMR and Force Field Investigations of Hydrindane Conformations†

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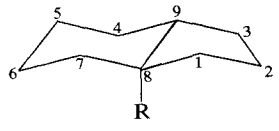
^{13}C NMR shifts of *trans*- and *cis*-annelated bicyclo[4.3.0]nonanes with substituents R in position 8 (R = H, OH, Cl, Br) and 1-hydroxy derivatives were analysed on the basis of force field calculated torsional angles using Allinger's MM1 program. Shielding increments for the 6 membered ring agree with corresponding cyclohexane values within ±0.8 ppm maximal deviation. ^{13}C NMR line shape analysis with *cis*-hydrindane between 148 and 180 K yielded $\Delta H^* = 37.0 \pm 0.4$ kJ mol^{-1} and $\Delta S^* = 28$ J mol^{-1} K^{-1} for the topomerization. The force field calculated reaction profile showed $\Delta H^* = 37$ kJ mol^{-1}, in close agreement.

INTRODUCTION

Bicyclo[4.3.0]nonanes provide an attractive testing ground for new methods in conformational analysis as they contain slightly distorted cyclohexane chairs, as well as cyclopentane, in restricted geometries.

They have been studied largely by chemical reactions and, to a lesser degree, by spectroscopic techniques;[2] the application of ^1H NMR methods in particular was severely hampered by the normally poor resolution.[3] We wanted to see to what degree ^{13}C NMR spectroscopy and molecular mechanics force field calculations could further the conformational analysis of these compounds, and yield information which could eventually also be applied to related systems such as the C/D rings of steroids.



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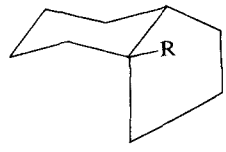
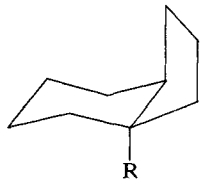


2a



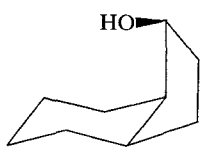
2b

RESULTS AND DISCUSSION

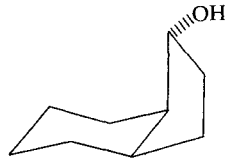
Compounds

Tertiary 8-hydroxy derivatives **1** and **2** (R = OH) were accessible by a recently developed regio- and stereospecific hydroxylation method[4] using the commercially available hydrocarbons **1** and **2** (R = H). Treatment of the alcohols **1** and **2** (R = OH) with oxalic acid yielded the $\Delta^{8,9}$ olefin, which was converted to epimeric mixtures of **1** and **2** (R = Cl, Br).[5]

Since catalytic hydrogenation of indanone[6] always led to substantial amounts of 1-indanol, the secondary alcohols **3** were obtained from mixtures of *cis*- and *trans*-hydrindan-1-one, which are formed by hydrogenation of hydrind-8,9-ene-1-one.[7] Both reduction with aluminium isopropylate/isopropanol and with lithium aluminium hydride leads predominantly to the more stable **3a** and **3d**, indicating a product controlled transition state as expected for the $LiAlH_4$ reaction on an unhindered ketone;[8] the Meerwein–Ponndorf–Verley reduction was accompanied by considerable isomerization on the ring junction, due to the α position of the carbonyl group.



3a



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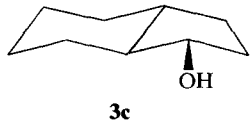
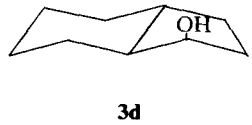


3c



3d

trans-Hydrindanes (1)

The *trans* annelated compounds are conformationally more homogeneous and can be expected to show, at least for the cyclohexane moiety, ^{13}C NMR shielding increments known from corresponding cyclohexyl compounds.[9] In fact, calculations using increments from 4-*tert*-butyl-1-methylcyclohexanes[9] yield experimental shifts with smaller deviations for the cyclohexane signals (C-4 to C-7) (1.4 ppm at most) than for the

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† Part 29 of Stereochemical and ^{13}C NMR Investigations. For Part 28, see Ref. 1.

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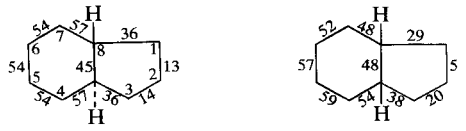

Figure 1. Force field calculated CCCC torsional angles (degrees) for *trans*- and *cis*-hydrindane.

signals of the geometrically different cyclopentane moiety (C-1 to C-3, C-8, C-9) (up to 5 ppm deviation). Force field calculations with Allinger's MM1 program[10] for **1** (R = H) indicate torsional angle deviations of only 2° from normal cyclohexane co-ordinates, except for the ring junction; the cyclopentane appears as a twisted half chair (Fig. 1).

cis-Hydrindanes (2)

The interconversion of *cis*-hydrindane topomers is expected to be faster than that of *cis*-decalin,[11] which involves a two-fold cyclohexane chair–chair inversion. (For ^{13}C DNMR measurements of *cis*-decalin, see Ref. 11(a).) A barrier of $\Delta G^* = 27$ kJ mol^{-1} has been estimated on the basis of poorly resolved ^{1}H NMR spectra at low temperature for **2** (R = H) using approximate methods.[12] Low temperature ^{13}C NMR spectroscopy can provide particularly accurate exchange rates if, as in the present case, no other variables such as equilibrium constants, in addition to the rate constants, are involved. Several exchanging signals can be used,[13] and non-exchanging signals (here: C-2) are

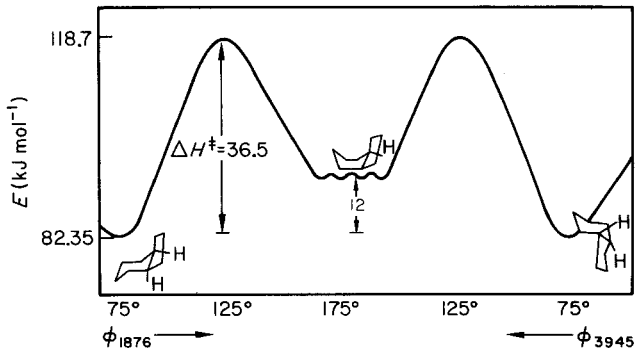

Figure 2. Force field calculated reaction profile for the *cis*-hydrindane inversion.

available for the estimation of the effective transverse relaxation time to be subtracted from the observed exchange broadened signals. Complete line shape analysis of all four exchanging signal pairs at eight temperatures between 148 and 180 K yielded an activation free enthalpy of 37.0 ± 0.4 kJ mol^{-1}, which can now be compared to force field calculated barriers.

A reaction profile for the *cis*-hydrindane inversion was constructed by MM1 energy minimization for 10 different structures, at fixed values for the C-1—C-8—C-7—C-6 torsional angle in steps of 10° between 75° and 175° (Fig. 2). The barrier thus calculated fits the experimental value within ±1 kJ mol^{-1} and supports the predictive power of the applied force field for conformational processes.

Introduction of substituents at the ring junction of **2** (R = OH, Cl, Br) leads to unequal populations of the

Table 1. ^{13}C NMR shifts in *trans*-hydrindanes[a]

		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
8-H		31.52	21.84	31.52	32.17	26.84	26.84	32.17	46.93	46.93
8-OH	Exp.	39.00	20.08	27.88	26.50*	25.67*	21.63	36.79†	78.32	47.96
	Calc.	34.83	15.06	26.50	27.15	26.57	21.82	35.48	83.19	50.24
8-Cl	Exp.	42.05†	20.20	27.95	26.45*	25.80*	21.96	39.06†	84.69	50.18
	Calc.	37.37	17.55	27.23	27.88	26.05	22.55	38.02	85.93	52.78
8-Br	Exp.	43.42†	20.28	28.66*	27.82*	25.60	22.88	40.30†	86.96	51.12
	Calc.	38.73	18.25	27.93	28.58	25.98	23.25	39.38	85.34	54.14
3d *trans–cis*-1-OH$_{ax}$		74.16	32.82†	30.40†	34.05†	26.71	26.71	26.58	52.51	41.27
3c *trans-trans*-1-OH$_{eq}$		77.60	32.82*	29.96†	32.69*	26.71	26.71	29.44†	54.01	43.61

[a]In ppm from internal TMS (10%), at 300 ± 10 K, (10 ± 5)% in $CDCl_3$. Signal assignments denoted by †* are mutually interchangeable.

Table 2. ^{13}C NMR shifts in *cis*-Hydrindanes[a]

		C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
8-H	300 K	27.57	22.30	27.57	29.57	23.59	23.59	29.57	39.45	39.45
8-H	142 K	27.04	22.30	27.88	26.45	25.93	20.86	32.82	39.45	40.04
8-OH	Exp.	35.35†	20.34	29.18‡	29.37‡	23.53*	24.17*	35.81†	80.92	46.79
8-OH$_{eq}$	Calc.	35.17	17.28	22.86	30.02	24.88	24.43	40.95	83.72	48.17
8-OH$_{ax}$	Calc.	31.19	25.87	30.57	27.80	20.59	20.91	29.76	76.30	42.76
8-Cl	Exp.	37.24†	20.41	28.53†	28.73†	23.40*	23.72*	38.87†	80.33	48.62
8-Cl$_{eq}$	Calc.	37.51	18.01	23.59	30.28	24.36	24.69	43.29	82.74	50.51
8-Cl$_{ax}$	Calc.	33.73	26.13	30.87	28.53	20.07	21.64	32.30	79.04	45.28
8-Br	Exp.	38.87†	20.86	28.47‡	28.92‡	23.33*	24.04*	40.30†	78.58	49.72
8-Br$_{eq}$	Calc.	37.57	18.71	24.29	30.60	24.29	25.01	43.35	79.89	50.57
8-Br$_{ax}$	Calc.	35.09	26.45	31.19	29.23	20.00	22.34	33.66	78.45	46.66
3d *cis–cis*-1-OH$_{ax}$		76.24	31.26	24.99†	24.63†	21.38	21.38	27.43	43.48	36.07
3b *cis–trans*-1-OH$_{eq}$		76.81	32.82	27.10†	25.15	23.78	22.94	27.82†	47.96	36.66

[a]In ppm from internal TMS (10%), at 300 ± 10 K, (10 ± 5%) in $CDCl_3$, except for 8-H in $CFCl_3/CF_2Cl_2$ (1:1). Signal assignments denoted by †‡* are mutually interchangeable.

invertomers **2a** and **2b** which should also be measureable by low temperature ^{13}C NMR spectroscopy. The lower barrier (e.g. $\Delta G^*_{148\,K} = 33\ kJ\ mol^{-1}$) and the lower solubilities of the substituted compounds around 140 K, however, prevented the use of this method. Time averaged shifts observed at room temperature can be analysed if shift values for the individual conformers **2a** and **2b** are available from model compounds. As described above for the *trans* series **1**, such values were also calculated for **2a** and **2b**, and can be compared to the observed shifts which, at least for the cyclohexane moiety, are between the shielding values of the models **2a** and **2b**. If one uses only signals which are unambiguously assigned, with a sufficiently large shift difference between **2a** and **2b** (e.g. C-5), application of Eliel's equation[2]

$$K = \frac{\delta_e - \delta_x}{\delta_x - \delta_a}$$

leads to approximately 70% **2a** and 30% **2b** for **2** (X = OH, Cl, Br). Thus, the equatorially substituted conformer with respect to the cyclohexane is more stable, but to a lesser degree than in monosubstituted cyclohexanes. This can be ascribed to the counterbalancing effect of alternative pseudo-axial substitution with respect to the cyclopentane ring in **2b**.

1-Hydroxyhydrindanes (3)

The 1-hydroxyhydrindanes **3** (Tables 1 and 2) contain the substituent in the cyclopentane ring, for which no reliable ^{13}C shielding increments at defined geometries are yet available. Introduction of the hydroxy groups deshields C-α by 43–50 ppm and C-β by 9–11 ppm. These effects are similar to those in cyclohexanes,[9] but will not allow configurational assignments at the present time. In contrast, and as usual in alicyclic compounds,[9,14] the γ-carbon shift reflects more clearly the orientation of the substituent. The C-γ shielding seems to increase with decreasing torsional angle φ (C-γ—C-β—C-α—O) from, for example, −3.3 ppm ($\varphi = 160°$, C-9 in **3b** and **3d**) to −4.0 and −5.6 ppm ($\varphi = 40$–$90°$, C-9 in **3a** and **3c**, C-7 in **3a–c**).

EXPERIMENTAL

^{13}C NMR spectra were recorded on a Bruker HX 90 spectrometer, with ^1H noise decoupling, at 22.63 MHz by the PFT technique using 20° pulse angles with 0.68 s acquisition time for 8/4 K spectra, yielding a digital resolution of 0.05 ppm. $CDCl_3$ or $CF_2Cl_2/CFCl_3$ were used as internal D or F lock, respectively. For measuring conditions, see Tables 1 and 2; the signal assignments given there are in accordance with multiplicities as observed in off-resonance decoupled spectra and with shifts calculated with increments from model compounds (see text).

Dynamic ^{13}C NMR studies were carried out with **2** (X = H) (5–10% in 50:50 $CFCl_2/CFCl_3$ mixtures) by visual comparison of experimental and computer simulated spectra (Fig. 3). The simulation was based on the uncoupled two-site exchange program by Binsch.[15] The probe temperature was controlled by a Bruker BST 100/760 unit, which was calibrated with a ^{13}C chemical shift thermometer[16] indicating deviations of $< 0.5°$. The following rates (in s^{-1}) were obtained: 148 K, 7.94; 152 K, 15.4; 156 K, 42.7; 160 K, 76.9; 164 K, 168.3; 168 K, 331; 176 K, 1052; 180 K, 3731. Linear regression yielded $\Delta H^* = 37 \pm 0.4$ (kJ mol^{-1}), $\Delta S^* = 28 \pm 3$ (kJ mol^{-1} K^{-1}), $\Delta G^*_{298\,K} = 28.7$ (kJ mol^{-1}).

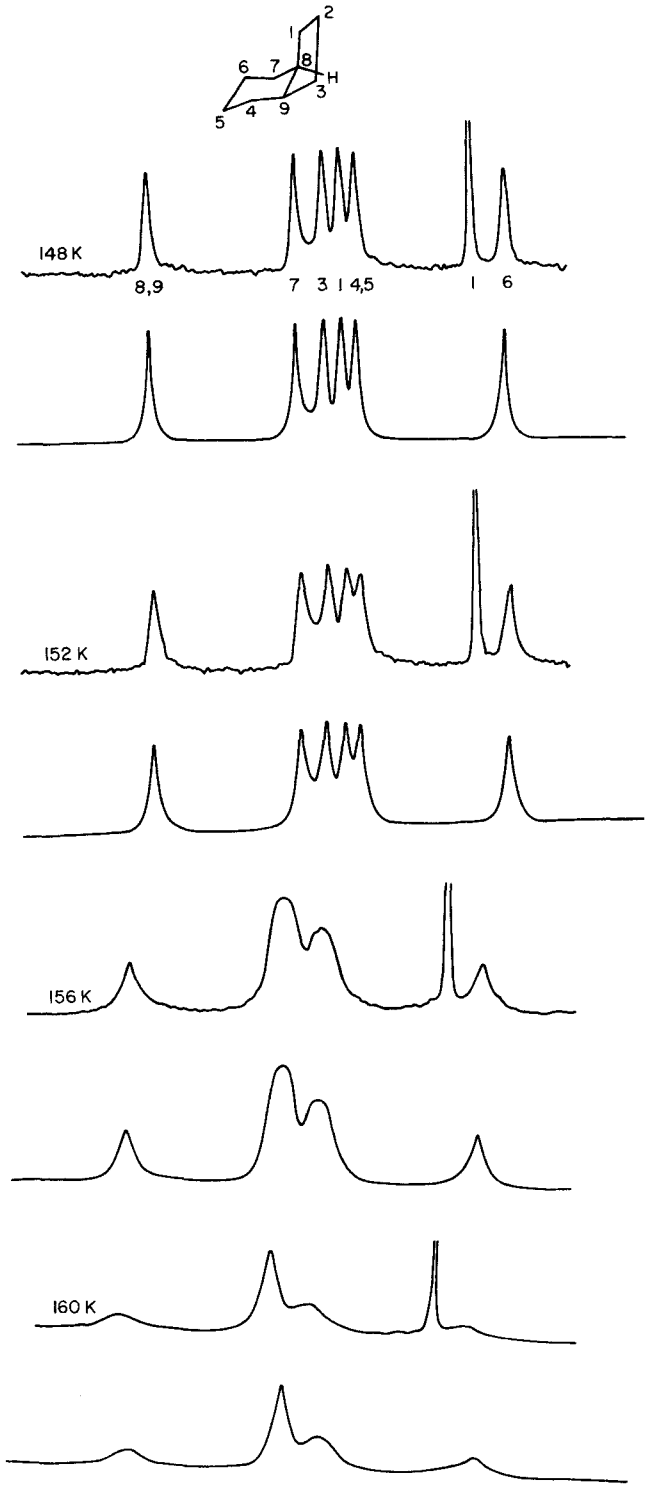

Figure 3. Experimental and simulated ^{13}C NMR line shapes for the *cis*-hydrindane inversion.

Calculations were carried out in FORTRAN on the Telefunken computer TR 440 of the Universität des Saarlandes. In the force field calculations energy minimizations were carried out until the final steric energy changed by <20 J mol^{-1}.

Coumpounds 1 and **2** (R = H) were obtained from commercially available mixtures, >99% pure for **2** (R = H), and as a 50:50 mixture for **1** (R = H) by fractionation on a 1 m spinning band column. **1** and **2** (R = OH): 18 g (0.145 mol) of the hydrocarbon mixture **1** and **2** (R = H) were refluxed in 40 ml chloroform with 26.5 g (0.145 mol) *p*-nitroperbenzoic acid for 1 day. After addition of more *p*-nitroperbenzoic acid (26.5 g) and prolonged heating for another day the solution was filtered, washed with aqueous sodium bicarbonate and water, and dried over sodium sulphate. The residue obtained after distillation of the solvent showed the presence of 10% nitrobenzene and by fractionation yielded 13 g alcohol (64%) at b.p.$_{0.1}$ 51°C; the product was further purified by sublimation. Reaction of the commercial hydrocarbon mixture (*c.* 85% *cis*) furnishes the pure *cis* product **2** (R = OH); the epimer was obtained from the 50:50 mixture of **1**, **2** (R = H). **1**, **2** (R = Cl, Br) were prepared from hydrind-8,9-ene according to the procedure of Becker and Grob.[5]

1-Hydrindanols 3 were obtained from an 80:20 mixture of *cis*- and *trans*-hydrindan-1-one.[7] For the Meerwein–Ponndorf–Verley (MPV) reduction, 6 g ketone were heated for 10 days with 5 g freshly prepared aluminium isopropylate in 100 ml isopropanol, and worked up as usual. The lithium aluminium hydride (LAH) reduction was carried out by standard procedures in refluxing ether. Gas–liquid chromatography ^{13}C NMR and ^{1}H NMR analysis yielded the following product composition.

	3a	**3b**	**3c**	**3d**	
MPV	35	5	25	35	%
LAH	60	20	<1	20	%

Acknowledgements

We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

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Received 18 June 1981; accepted 7 September 1981

Notes added in proof

(a) A recent calculation using the Ermer–Lifson force field, supported by electron diffraction results, agrees with out torsional angles for **1, 2** (R = H) within ±1°; L. Van den Enden and H.-J. Geise, *J. Mol. Struct.* **74,** 309 (1981).

(b) For a recent ^{13}C NMR study of oxa- and thia-hydrindanes see R. L. Willer, *Org. Magn. Reson.* **16,** 261 (1981).