

Synthesis and Conformational Analysis of 3-Methyl-3-silatetrahydropyran by GED, FTIR, NMR, and Theoretical Calculations: Comparative Analysis of 1-Hetero-3-methyl-3-silacyclohexanes

Bagrat A. Shainyan,^{*,†} Svetlana V. Kirpichenko,[†] Nina N. Chipanina,[†] Larisa P. Oznobikhina,[†] Erich Kleinpeter,[‡] Sergey A. Shlykov,[§] and Dmitriy Yu. Osadchiy[§]

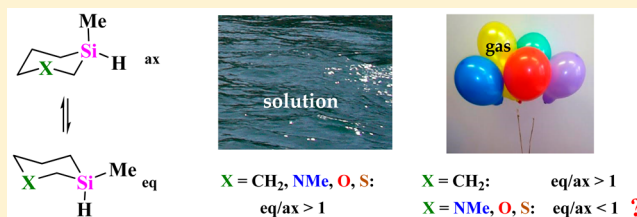
[†]A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Division of the Russian Academy of Sciences, 1 Favorsky Street, Irkutsk 664033, Russian Federation

[‡]Chemisches Institut der Universität Potsdam, Karl-Liebknecht-Strasse 24-25, Potsdam (Golm) D-14476, Germany

[§]Ivanovo State University of Chemistry and Technology, Research Institute for Thermodynamics and Kinetics of Chemical Processes, Sheremetev avenue 7, Ivanovo 153000, Russian Federation

Supporting Information

ABSTRACT: 3-Methyl-3-silatetrahydropyran **1** was synthesized and its molecular structure and conformational behavior was studied by gas-phase electron diffraction (GED), FTIR, low temperature ¹H and ¹³C NMR spectroscopy, and by theoretical calculations (DFT, MP2). Two conformers, **1-ax** and **1-eq**, were located on the potential energy surface. In the gas phase, a slight predominance of the axial conformer was determined, with the ratio **1-ax:1-eq** = 54(9):46(9) (from GED) or 53:47 or 61:39 (from IR). In solution, LT NMR spectroscopy at 103 K gives the ratio **1-ax:1-eq** = 35:65 ($-\Delta G_{103}^{\circ} = 0.13$ kcal/mol). Simulation of solvent effects using the PCM continuum model or by calculation of the corresponding solvent–solute complexes allowed us to rationalize the experimentally observed opposite conformational predominance of the conformers of 3-methyl-3-silatetrahydropyran in the gas phase and in solution. Comparative analysis of the effect of heteroatom in 1-hetero-3-methyl-3-silacyclohexanes on the structure, stereoelectronic interactions, and relative energies of the conformers is done.



INTRODUCTION

The well-established preference of most substituents to occupy the equatorial position in a cyclohexane ring is a general rule, which can be violated only in very specific cases.¹ To the best of our knowledge, only one exception was reported, an O-cyclohexyl oxime of complex structure, which was declared as the “first completely stable axial conformer of monosubstituted cyclohexanes”.² Its stability was assigned to strong destabilization of the corresponding equatorial conformer by steric hindrances with the side chain of the oxime moiety. However, this was immediately disproven by Cornett et al.,³ who came to the conclusion that the authors dealt with the rapidly exchanged mixture of the corresponding axial and equatorial conformers. Also, the preference of axial OH conformers was demonstrated by Rittner et al. for cyclohexanols capable of formation of intramolecular H-bonds with 3-OMe⁴ or 3-NMe₂⁵ substituents. Up to 32% of the axial conformer was detected in the conformational equilibrium of the cyclohexyl esters RCOOC₆H_{11-c} with more and more electronegative substituents R.⁶ Further, the “equatorial rule” is occasionally reversed in O-heterocycles bearing an electronegative group at the carbon adjacent to the endocyclic oxygen atom.⁷

Conformational preferences of the substituents more remote from the heteroatom, like that in 3-substituted monohetero-

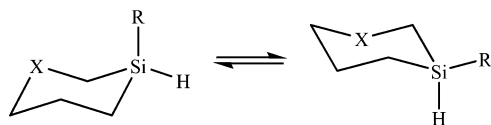
ocyclohexanes, are affected by homoanomeric effects, which were examined in detail by Alabugin et al.,⁸ and in a specific case of methylheterocyclohexanes by Ribeiro and Rittner.⁹ Although these effects are considerably weaker than vicinal orbital interactions which are responsible for the classical anomeric effect,⁸ they may be important for 3-substituted oxanes, piperidines, thianes, and related compounds. Thus, the conformational free energy (A value) for the methyl group in cyclohexane (1.76 kcal/mol)¹⁰ is reduced in 3-methyltetrahydropyran (1.44 kcal/mol),¹¹ 3-methylthiane (1.4 kcal/mol),¹² 3-methylpiperidine, and 1,3-dimethylpiperidine (1.6 kcal/mol),¹³ being, however, still strongly in favor of the equatorial conformer. The usual explanation for this decrease is the substitution of a *syn* axial H—H repulsion by a H/lone pair repulsion, which is thought to be less severe.¹⁴ Alternatively, when studying the conformational equilibria of 1,4-disubstituted cyclohexanes¹⁵ and 4-substituted cyclohexanes¹⁶ with substituents of variable polarity, it was proven: *The more polar the substituents, the more polar the six-membered ring moiety and the more polar the whole molecule become, respectively, the more stable the axial conformer with respect to its equatorial analog.*

Received: October 12, 2015

Published: November 20, 2015

The situation changes drastically when going from cyclohexanes or their oxygen, nitrogen, or sulfur heteroanalogs to silacyclohexanes or silaheterocyclohexanes. The conformational behavior of the Si-monosubstituted silacyclohexanes was studied for halogens,^{17–19} CF₃,^{20,21} SiH₃,²² Me,^{21,23} *t*-Bu,²⁴ and Ph^{25,26} as substituents (Scheme 1).

Scheme 1



$$A = -\Delta G^0 = G_{\text{ax}} - G_{\text{eq}} = RT \ln(K)$$

X = CH₂; **R** = Hal, CF₃, SiH₃, Me, *t*-Bu, Ph.
X = S, NMe; **R** = Me.

It was unequivocally established that all electronegative substituents at silicon, even the bulky CF₃ group, prefer the axial orientation, which was assigned to less steric hindrances and more favorable stereoelectronic orbital interactions in the axial conformers.²⁶

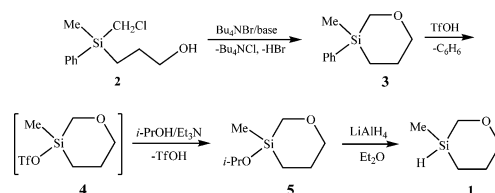
The methyl group is the reference substituent in conformational analysis (actually, it is common to adjust the effects of all other substituents with that of the methyl group). Inasmuch as the conformational analysis was already performed for 1-methylsilacyclohexane,^{21,23} 1,3-dimethyl-3-silapiperidine,²⁷ and 3-methyl-3-silathiane (Scheme 1),^{28,29} the only missing link in the series of the studied silaheterocyclohexanes is 3-methyl-3-silatetrahydropyran **1**. The corresponding study will throw light on the anomeric (homoanomeric) effect in sila(hetero)cyclohexanes. So far, the presence of a “stereoelectronic effect, similar to the anomeric effect” was mentioned only for silacyclohexanes.³⁰ Therefore, one major goal of the present study is to fill this gap.

Another interesting aspect proves to be the comparison of conformational preferences in the gas phase and in solution. Results obtained so far for Si-monosubstituted silacyclohexanes and silaheterocyclohexanes^{17–29} lead to the conclusion that electronegative substituents at silicon further increase their inherent axial preference on going from the gas phase to the solution.^{17,18,20} By contrast, in the equatorially favored 1-Me and 1-Ph-1-silacyclohexanes, the population of the axial conformer in solution is less than that in the gas phase.^{23,25,26} For 1-SiH₃-1-silacyclohexane, the axial preference in the gas phase is reversed to the equatorial preference in solution.²² 1,3-Dimethyl-3-silapiperidine²⁷ and 3-methyl-3-silathiane^{28,29} show an explicit inversion of conformational preferences from the predominant axial conformer in the gas phase to the predominant equatorial conformer in solution. This motivated the second goal of our study, which was to analyze the dependence of conformational preferences of the methyl group on the nature of the second heteroatom in silaheterocyclohexanes. Finally, it was of interest to compare the results of different methods having different characteristic time scales, like NMR and FTIR spectroscopy with transitions in the millisecond and picosecond domains. All together, in this study, we report synthesis, molecular structure, and conformational analysis of 3-methyl-3-silatetrahydropyran **1** by gas-phase electron diffraction, FTIR, and low temperature NMR spectroscopy and by theoretical calculations.

RESULTS AND DISCUSSION

Synthesis. 3-Methyl-3-silatetrahydropyran **1** was synthesized by a multistep procedure (Scheme 2) starting from

Scheme 2



chloromethyl(3-hydroxypropyl)methyl(phenyl)silane **2**, which was cyclized to 3-methyl-3-phenyl-3-silatetrahydropyran **3**. Dephenylation of **3** via the intermediate (not isolated) triflate **4** gave 3-methyl-3-*iso*-propoxy-3-silatetrahydropyran **5**,³¹ which was finally reduced with lithium aluminum hydride to the target product **1** in 50% yield.

The procedure in Scheme 2 is analogous to that used for the synthesis of the similarly substituted S-cycle, 3-methyl-3-silathiane,²⁹ but different from the alternative scheme used for the synthesis of the corresponding N-cycle, 1,3-dimethyl-3-silapiperidine, which was based on cyclization of the prefunctionalized substrate, (chloromethyl)(3-chloropropyl) (*iso*-propoxy)methylsilane.²⁷ The choice of the method was dictated by the fact that functionalization at silicon proceeds in better yield for cyclic substrates (as was applied in the case of the O- and S-cycles) but is complicated by the triflic salt formation in the case of the N-cycle.

GED Analysis. The refinement of the structure and the relative amount of the conformers was carried out by the least-squares analysis of the experimental molecular scattering intensity *sM*(*s*) curves. Quantum chemical calculations revealed two stable conformers of compound **1** having the chair conformation and differing in the axial or equatorial location of the methyl group (Figure 1). The selected experimental geometric parameters are given in Table 1 together with the calculated geometry.

Experimental and theoretical molecular scattering intensity *sM*(*s*) curves along with the differences “Experim.–Theor.,” $\Delta sM(s)$, are given in Figure 2.

The 18 independent geometric parameters of the **1-eq** conformer were refined simultaneously and independently, together with 4 groups of vibrational amplitudes and with the conformer ratio. The geometric parameters for the **1-ax** conformer were described by the parameters analogous to those for **1-eq** conformer and corrected by adding the differences taken from MP2/6-311G** calculations. The other geometric parameters were described using differences with the homologous ones adopted from the MP2/6-311G** calculations.

Comparison of the radial distribution curves *f*(*r*) and differences $\Delta f(r)$ curves “Experim.–Theor.” in Figure 3 suggests that both conformers are present in the vapor under the conditions of the GED experiment.

An attempt to describe the experimental scattering intensities under the assumption that the vapor contains only one of the conformers yielded the agreement factor *R_f* values of 9.2 and 10.6% without refinement (MP2/6-311G**), 5.5 and 5.7% with refinement of all structural parameters, for **1-ax** and **1-eq**, respectively. The least-squares refinement of the conformer

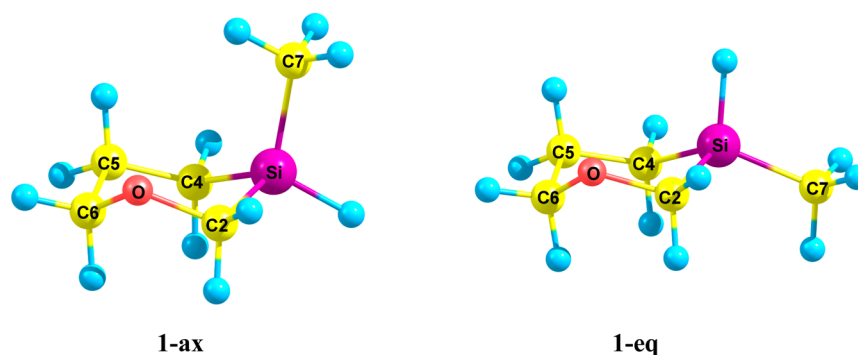


Figure 1. Molecular structure of the axial and equatorial conformers of 3-methyl-3-silatetrahydropyran 1.

Table 1. Selected Calculated and Experimental (GED) Geometrical Parameters for Conformers 1-ax and 1-eq^a

parameter	GED ^b	1-ax			1-eq		
		B3LYP 6-311G**	MP2		B3LYP 6-311G**	MP2	
			cc-pVTZ	6-311G**		cc-pVTZ	6-311G**
bond lengths							
O—C2	1.441(3)	1.441	1.439	1.440	1.439	1.436	1.438
C2—Si	1.895(4)	1.907	1.898	1.897	1.907	1.898	1.897
Si—C4	1.881(4)	1.896	1.886	1.885	1.894	1.884	1.884
C4—C5	1.541(4)	1.546	1.536	1.542	1.545	1.536	1.541
C5—C6	1.529(4)	1.533	1.523	1.530	1.533	1.524	1.529
C6—O	1.422(3)	1.424	1.420	1.420	1.423	1.419	1.419
Si—H	1.483 ^c	1.493	1.487	1.485	1.491	1.486	1.483
Si—C _{Me}	1.876(4)	1.885	1.876	1.876	1.886	1.879	1.878
bond angles							
O—C2—Si	109.9(5)	109.1	108.0	108.2	109.6	109.4	109.3
C2—Si—C4	101.9(9)	101.8	101.4	101.5	102.1	101.7	101.8
Si—C4—C5	110.4(5)	111.0	109.7	109.9	110.8	109.7	110.0
C4—C5—C6	111.8(5)	113.5	112.8	112.9	113.4	112.8	112.9
C5—C6—O	115.4(8)	113.7	113.7	113.6	113.7	113.8	113.6
C6—O—C2	113.2(8)	113.8	112.4	112.1	113.9	112.5	112.2
C2—Si—C _{Me}	112.6(9)	111.0	111.8	113.0	113.0	111.3	113.0
H—Si—C _{Me}	107.6 ^d	109.6	110.5	110.3	109.6	110.3	110.0
dihedral angles							
O—C2—Si—C4	47.4(22)	46.9	49.0	48.2	45.6	49.0	48.2
C2—Si—C4—C5	-43.6(24)	-40.9	-44.0	-42.0	-40.3	-44.0	-42.0
Si—C4—C5—C6	-52.5(19)	-49.9	-52.1	-51.3	-50.3	-52.5	-51.4
C4—C5—C6—O	65.6(22)	64.0	65.9	65.5	65.0	67.0	66.4
C5—C6—O—C2	-71.8(14)	-73.6	-75.0	-75.2	-73.4	-74.2	-74.7
C6—O—C2—Si	62.1(11)	65.0	66.7	67.1	63.4	64.6	65.5

^aDistances in Å, angles in degrees; r_e and \angle_e values (calculations) and r_{h1} ($r_{h1} = r_a + \Delta r$) and \angle_{h1} (GED) are given. The latter were derived by using the vibrational correction Δr calculated in harmonic approximation using SHRINK program^{32,33} on the basis of the force field estimated by quantum chemical calculations at the MP2/6-311G** level. ^bFor the 1-eq conformer. Geometry of the 1-ax conformer is very close (see Supporting Information, SI). Values in parentheses for the GED data are full errors estimated as $\sigma(r_{h1}) = [\sigma_{scale}^2 + (2.5\sigma_{LS})^2]^{1/2}$, where $\sigma_{scale} = 0.002r$ and σ_{LS} is a standard deviation in least-squares refinement for internuclear distances and as $3\sigma_{LS}$ for angles. The place-value is such that the last digit of the uncertainty lines up with the last digit of the nominal value. ^cFixed value. ^dDependent parameter.

ratio along with all geometric and vibrational parameters converged at 1-ax:1-eq = 54(5):46(5), where $3\sigma_{LS}$ is given in parentheses, $R_f = 3.4\%$.

From the plot in Figure 4, the relative contribution of the conformers is 1-ax:1-eq = 54(9):46(9) %, that corresponds to the A value of $-0.09(22)$ kcal/mol at 286 K.

The relative energies and Gibbs energies of the conformers are summarized in Table 2.

Approximately equal amounts of the conformers in the gas phase are predicted by DFT calculations with $-\Delta G^\circ(298\text{ K})$ from -0.01 to -0.04 kcal/mol, practically coinciding with the

GED experimental value of $-\Delta G^\circ(286\text{ K}) = -0.09$ kcal/mol. The MP2 method gives a larger prevalence of the axial conformer but may also be considered as agreeing with the GED data within the error of the experiment. Note that for the recently studied 1,3-dimethyl-3-silapiperidine²⁷ and 3-methyl-3-silathiane,²⁹ the DFT and MP2 calculations also predicted different prevalence of the axial and equatorial conformers, while for their predecessor, 1-methyl-1-silacyclohexane, all experimental and theoretical methods give the predominance of the equatorial conformer^{21,23,35} (except for apparently erroneous conclusion in an old paper).³⁶

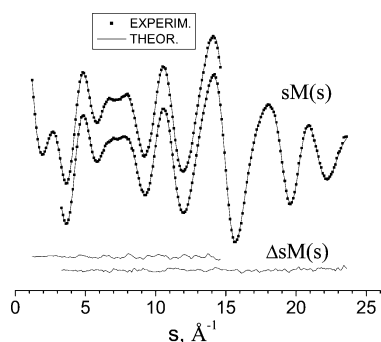


Figure 2. Molecular scattering intensities $sM(s)$: experimental (dots) and theoretical (line) for the refined mixture of the conformers **1-ax:1-eq** = 54(9):46(9); the difference “Experim.–Theor.” is given at the bottom.

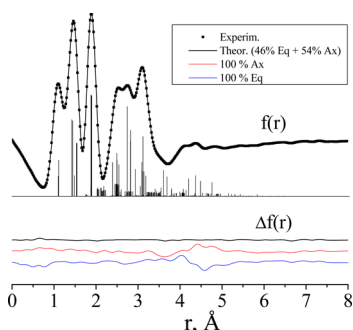


Figure 3. Radial distribution curves: experimental (black dots) and theoretical (black line) for refined mixture of the conformers **1-ax:1-eq** = 54(9):46(9); colored lines are the theoretical curves obtained at refinement under assumptions of the individual conformers; the differences “Experim.–Theor.” are given at the bottom.

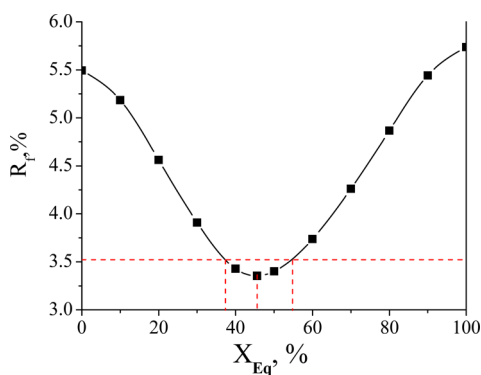


Figure 4. Agreement factor R_f as a function of molar fraction of the **1-eq** conformer. The horizontal line corresponds to the Hamilton's criterion³⁴ at a 0.05 significance level.

The endocyclic Si—C2 and Si—C4 bond lengths, 1.895(4) and 1.881(4) Å, respectively, in both conformers of **1** are in excellent agreement with those in 3-methyl-3-phenyl-3-silatetrahydropyran, 1.897(4) and 1.883(4) Å.³⁷ Note that in the nitrogen analog, 1,3-dimethyl-3-silapiperidine, the GED determined lengths²⁷ of the Si—C2 and Si—C4 bonds within the error of the experiment coincide with the above values for **1**. At the same time, the Si—C2 and Si—C4 bond lengths in 3-methyl-3-silathiane²⁹ are equal, and reproduce the Si—C4, but are slightly shorter, by ca. 0.015 Å, than the Si—C2 distance, in **1**. Thus, the O or N heteroatom in **1** or in its nitrogen analog elongate the neighboring Si—C2 bond with respect to that in

3-methyl-3-silathiane. The reasons for that are, however, different. The NBO analysis of molecule **1** showed that weakening (and, hence, elongation) of the Si—C2 bond in **1** is mainly due to $(n_{O1} + n_{O2}) \rightarrow \sigma^*_{Si-C2}$ interaction and partly to $\sigma_{Si-C2} \rightarrow \sigma^*_{O-C6}$ hyperconjugation, which in total amount to 5.5 kcal/mol (for both conformers). In contrast, the NBO analysis of 1,3-dimethyl-3-silapiperidine we performed on the optimized geometry from ref 27 showed that for both conformers the former effect ($n_N \rightarrow \sigma^*_{Si-C2}$) is lacking (apparently, due to close-to-orthogonal arrangement of the corresponding orbitals), and the latter one is much larger: $E^{(2)}(\sigma_{Si-C2} \rightarrow \sigma^*_{N-C6}) = 4.9$ kcal/mol. In 3-methyl-3-silathiane, for both conformers, the former effect is rather low, $E^{(2)}(n_S \rightarrow \sigma^*_{Si-C2}) = 3.0 \pm 0.3$ kcal/mol, and the latter effect is lacking. This analysis allows us to account for the observed structural differences of 3-methyl-3-silaheterocyclohexanes in refs 27 and 29 and in the present study. The above orbital interactions in 3-methyl-3-silaheterocyclohexanes are also responsible for a longer Si—C (especially Si—C2) bond length in their molecules with respect to the endocyclic Si—C bond in 1-methyl-1-silacyclohexane (1.867 Å), in which such interactions are either absent or weak.²³

In general, geometric parameters of both conformers of **1** are in excellent agreement with those in 3-methyl-3-phenyl-3-silatetrahydropyran³⁷ except the C2—Si—C4 bond angle, which is reduced by 2° on going from mono- to disubstituted 3-silatetrahydropyran. The exocyclic Si—C bond lengths of 1.876 Å are by ca. 0.01–0.02 Å shorter than their endocyclic counterparts in this type of compounds.³⁷ The silicon atom in the molecule of 3-methyl-3-silatetrahydropyran **1** notably affects the degree of folding of the molecule with respect to tetrahydropyran.³⁸ The angle formed by the mean plane O1C2C4C5 with the C2C3C4 plane in tetrahydropyran is ca. 40°, and that with the O1C6C5 plane is ca. 55°. The corresponding angles with the C2SiC4 and OC6C5 planes in molecule **1** are ca. 35° and 65°, that is, the silicon increases the degree of folding in the “C-part” and decreases it in the “Si-part”.

Experimental GED parameters of **1** are in excellent agreement with the results of MP2 calculations, whereas some bond distances predicted by the DFT method tend to be overestimated by ~ 0.01 Å.

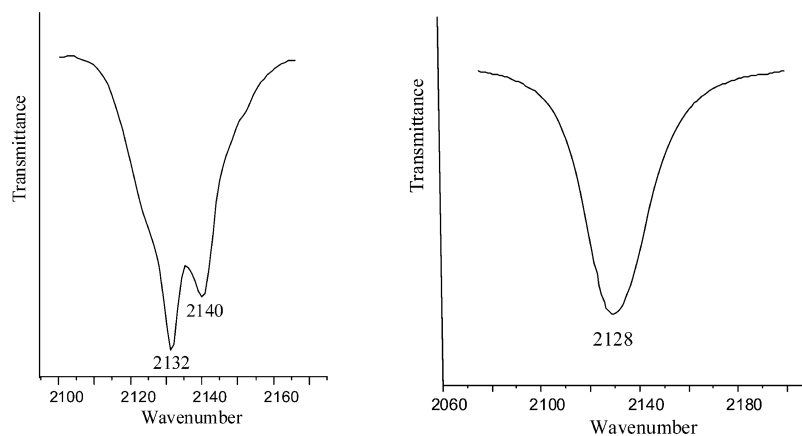
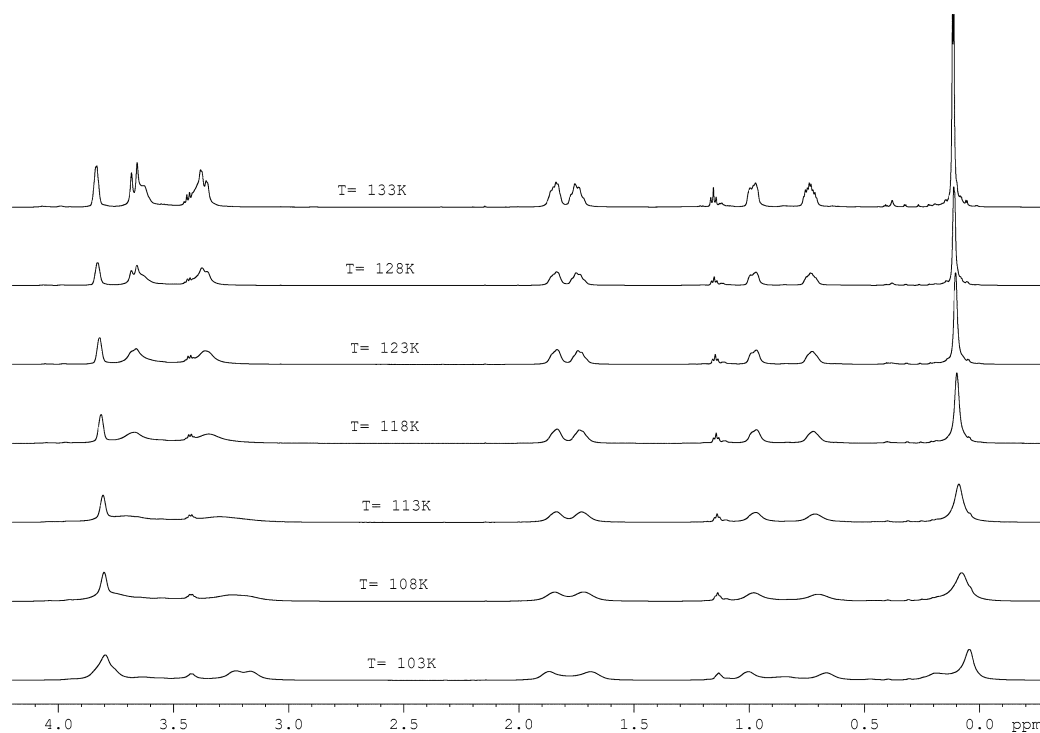
IR Spectroscopy. The FTIR spectroscopic study of 3-methyl-3-silatetrahydropyran **1** was performed in gas phase, in liquid state and in solution (for full spectra, see the SI). The gas phase spectrum of **1** at 296 K showed an intense doublet band with maxima at 2132 and 2140 cm^{-1} (Figure 5, left) assigned to Si—H stretching vibrations in **1-ax** and **1-eq**, respectively, based on normal mode calculations, similar to the earlier reported for 1,3-dimethyl-3-silapiperidine²⁷ and 3-methyl-3-silathiane.²⁹ The experimental difference $\Delta\nu(\text{Si—H}) = 8 \text{ cm}^{-1}$ is excellently reproduced by vibrational calculations being 9 cm^{-1} for the isolated molecules at the most sophisticated MP2/cc-pVTZ level of theory.

A higher intensity of the low-frequency component is indicative of a higher content of the **1-ax** conformer. The analysis of the peak and integral intensities after graphical separation of the overlapping bands gave the ratio **1-ax:1-eq** = 53:47 and 61:39, respectively, both being consistent with the GED determined ratio of 54(9):46(9).

In the FTIR spectrum of **1** in heptane solution at 296 K, a slightly asymmetric strong band at 2128 cm^{-1} , common for both conformers (Figure 5, right) is observed. Lowering the

Table 2. Relative Energies and Gibbs Energies (kcal/mol) for Conformational Equilibrium 1-ax \rightleftharpoons 1-eq

method	ΔE	$-\Delta G^\circ_{298\text{ K}}$	$-\Delta G^\circ_{103\text{ K}}$	$-\Delta G^\circ(\text{exp})$
B3LYP/6-311G(d,p)	0.06	-0.04	-0.04	(gas, GED, 286 K) - 0.09(22)
B3LYP/cc-pVTZ	0.03	-0.01	-0.02	
MP2/6-311G(d,p)	0.36	-0.34	-0.34	
MP2/cc-pVTZ	0.40	-0.33	-0.39	
MP2/6-311G(d,p)-PCM-CH ₂ Cl ₂	-1.76	1.94	1.95	(solution, LT NMR, 103 K) 0.13
B3LYP/cc-pVTZ-PCM-CH ₂ Cl ₂	-0.21	0.22	0.21	
+ CH ₂ Cl ₂ , MP2/6-311G(d,p)	0.26	-0.29	-0.27	
+ CHCl ₃ , MP2/6-311G(d,p)	0.26	-0.34	-0.28	
+ CH ₂ Cl ₂ , MP2/6-311G(d,p), PCM	0.03	-0.20	-0.09	
+ CHCl ₃ , MP2/6-311G(d,p), PCM	0.09	0.24	0.03	

Figure 5. FTIR spectra of compound **1** in the region of Si—H vibrations at room temperature: in gas (left); in heptane (right).Figure 6. ¹H NMR spectrum of 3-methyl-3-silatetrahydropyran **1** at various temperatures in CD₂Cl₂/CHCl₂F/CHClF₂.

solution temperature does not change its shape. A similar single band $\nu(\text{Si—H})$ at 2128 cm⁻¹ was observed in the heptane solution of the nitrogen analog of **1**, 1,3-dimethyl-3-silapiperidine.²⁷ Note that in gas phase, the frequency difference $\Delta\nu$ between the axial and equatorial conformers of

1,3-dimethyl-3-silapiperidine (6 cm⁻¹)²⁷ is very close to that for compound **1** (8 cm⁻¹). In the sulfur analog, 3-methyl-3-silathiane,²⁹ the value of $\Delta\nu$ in gas phase increases to 22 cm⁻¹. As a result, in heptane solution of 3-methyl-3-silathiane at 296 K, unlike the N- and O-analogs, the $\nu(\text{Si—H})$ band also

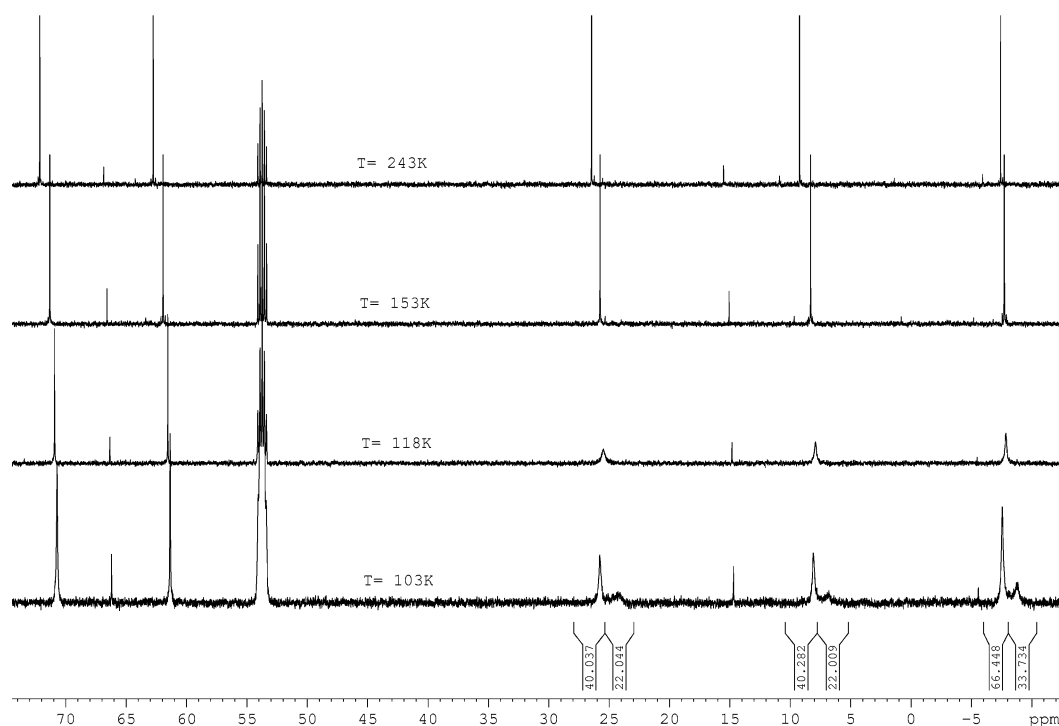


Figure 7. ¹³C NMR spectrum of 3-methyl-3-silatetrahydropyran **1** at various temperatures in CD₂Cl₂/CHCl₂F/CHClF₂.

appears as a clear doublet with maxima at 2118 (1-ax) and 2134 cm⁻¹ (1-eq), the intensity of the low-frequency component being increased with lowering the temperature.

In the spectra of the neat liquid and of the solution of **1** in CH₂Cl₂, the ν(Si—H) bands at 2123 and 2126 cm⁻¹, respectively, are single and symmetric as in the corresponding spectra of 1,3-dimethyl-3-silapiperidine²⁷ and 3-methyl-3-silathiane.²⁹ They are shifted by 2–5 cm⁻¹ to low frequencies relative to the band of the axial conformer in the gas phase, as could be expected in a more polar medium. According to MP2/6-311G(d,p) calculations, the low-frequency shift of ν(Si—H) band in 1-ax in CH₂Cl₂ is 10–12 cm⁻¹, whereas in 1-eq, it reaches 19–21 cm⁻¹, so that the ν(Si—H) values for the two conformers in CH₂Cl₂ become practically identical. With this in mind, the singlet bands observed in the spectra of solutions of compound **1** in CH₂Cl₂ and in neat liquid is considered as belonging to the equilibrium mixture of the two conformers with superimposed bands.

Low Temperature NMR Spectroscopy Study. Room temperature ¹H and ¹³C NMR spectra are shown in Figures S5 and S6. Temperature-variable ¹H and ¹³C NMR spectra from 243 to 103 K are shown in Figures 6 and 7, respectively. Both spectra were assigned in complete agreement with the HSQC experiment; the characteristic absorption ranges of both proton and carbon signals are specific enough to unequivocally assign the spectra and are in complete agreement with former studies (cf. Table 3). At low temperatures, all ¹³C signals are slightly shifted upfield. The SiMe, C4, and C5 signals broaden below 118 K and decoalesce at 103 K into two signals each (cf. Table 3 and Figure 7). First, the signals were assigned to SiMe_{ax} and SiMe_{eq} based on the well-known general principles of ¹³C NMR stereoanalysis and in accordance with the general rule that axial methyl substituents resonate at higher field than their equatorial analogs.^{1,11,13,38,39} According to the corresponding signal intensities C4 and C5 signals were adequately assigned. In addition (see Figure 6), and also in agreement with another

Table 3. ¹³C NMR Spectra of **1** at Various Temperatures in CD₂Cl₂/CHCl₂F/CHClF₂

T/K, conformer	δ(¹³ C), ppm				
	MeSi	2-CH ₂	4-CH ₂	5-CH ₂	6-CH ₂
298 (CDCl ₃)	-7.3	62.1	8.6	25.5	71.4
103, 1-ax, minor	-8.8 ^a	61.3 ^b	6.8 ^a	24.2 ^a	70.7 ^b
103, 1-eq, major	-7.6 ^a	61.3 ^b	8.1 ^a	25.8 ^a	70.7 ^b

^aDecoalescence, signals still broadened (Figure 7). ^bNo decoalescence yet, signals still sharp (Figure 7).

well-known stereoanalysis principle, the axial methyl ¹H resonance (at 103 K) is observed at low field (only due to this lowest temperature obtained, complete decoalescence could not be reached). Actually, the ratio between the two conformers looks very similar, as could be concluded from the detailed low temperature ¹³C NMR study (vide infra).

Because the decoalesced signals of SiMe, C4, and C5 are still rather broadened at 103 K integration of the separated signals can be processed only with some margin of error. While these results prove to be for C5 (64.5% 1-eq) and C4 (64.8% 1-eq) quite similar, the ratio obtained for SiMe is some different (66.5% 1-ax); however, due to residual signal broadening in between the conformer resonances return to the baseline could not be completely obtained.

The integration of the ¹³C signals of the three sets of signals allows us to determine the 1-ax to 1-eq conformer ratio (employing the mean value of integration of the three sets: 35:65%) and the equilibrium constant $K = 1.86$, which corresponds to the free energy difference $-\Delta G^\circ = 0.13 \pm 0.1$ kcal/mol in favor of equatorial conformer. This value is significantly less than that for 3-methyltetrahydropyran (1.44 kcal/mol, 173 K, CD₂Cl₂)¹¹ but very close to the values for already known Si-methylated heterocycles: 1-methyl-1-silylclohexane ($-\Delta G^\circ = 0.23$ kcal/mol),²³ 1,3-dimethyl-3-silapiper-

idine ($-\Delta G^\circ = 0.22$ kcal/mol)²⁷ and 3-methyl-3-silathiane ($-\Delta G^\circ = 0.35$ kcal/mol).²⁹

The results available now for 1-methyl-1-silacyclohexane and its heteroanalogues with N, O, and S heteroatoms in the β -position to silicon allows us to discuss the dependence of conformational preferences of the methyl group on the second heteroatom in silaheterocyclohexanes in the isolated molecules and in solution.

The results are summarized in Table 4, from which four points of interest can be obtained. The first one is the already

Table 4. Conformational Ratio 1-ax:1-eq and Free Energy Difference ΔG° (kcal/mol) in Gas Phase and in Solution for 1-Methyl-1-silacyclohexane and 3-Methyl-3-silaheterocyclohexanes

X	GED		LT NMR		ref
	1-ax:1-eq	$-\Delta G^\circ$	1-ax:1-eq	$-\Delta G^\circ$	
CH ₂	32:68	0.45	26:74	0.23	23
MeN	65:35	-0.36	32:68	0.22	27
O	54:46	-0.09	35:65	0.13	this work
S	60:40	-0.17	15:85	0.35	28, 29

well-known difference from methylcyclohexane, in which ax:eq = 0:100, explained by much less steric strains in silacyclohexanes. The second is the increase of the axial conformer population in 3-methyl-3-silaheterocyclohexanes vs 1-methyl-1-silacyclohexane in gas phase, up to the reverse of the ax:eq ratio. This can be tentatively assigned to stabilization of the axial conformer by attractive interaction of the methyl hydrogens with the heteroatom lone pair. Third, a slight increase of the ax:eq ratio in favor of the equatorial conformer in going from gas to solution for 1-methyl-1-silacyclohexane and its drastic increase leading to the reverse of the ratio in the case of 3-methyl-3-silaheterocyclohexanes (Table 4) is indicative of the effect of specific solvation, apparently with participation of the heteroatom lone pair since the dipole moments of the ax and eq conformers are not much different and hardly may cause any strong effect of solvent polarity. Finally, it is noteworthy that an increase of the ax:eq quotient in solution on going from 1-methyl-1-silacyclohexane to the N- and O-substituted analogs from 0.35 to 0.47 and 0.54 and its decrease to 0.18 for 3-methyl-3-silathiane. We assume that this might be due to a weaker aforementioned interaction of the methyl hydrogens with the more diffuse sulfur lone pair and, hence, a relative stabilization of the equatorial conformer.

The rate constant and the barrier to ring inversion of 3-methyl-3-silatetrahydropyran **1** were determined from the line shape variation of the ¹³C NMR signal of the Si–Me group in the temperature range down to 103 K. The corresponding dynamic NMR parameters were determined ($T_c = 109$ K, $\Delta\nu = 740$ Hz (SiMe), 750 Hz (C4), and 760 Hz (C5), mean value 750 Hz; $k_c = 1666$, population difference neglected) and the barrier to ring inversion was determined at T_c employing the usual approximations ($k_c = \pi \Delta\nu / \sqrt{2}$; $\Delta G^\ddagger = 19.14 T_c (10.42 + \log T_c/k_c)$). The Gibbs free energy of activation ΔG_c^\ddagger proves to be 4.6 kcal/mol, in good agreement with the barriers obtained for some other silaheterocyclohexanes.^{29,37,40,41} The population difference between the two participating conformers 1-ax and 1-eq was neglected; together with an experimental margin of

error; however, the barrier to ring interconversion of 4.6 ± 0.2 kcal/mol for compound **1** can be proven.

This is considerably lower than that in tetrahydropyran (10.3 kcal/mol, CH₃OD/CHClF₂)⁴² due to the aforementioned specific structural features of silacyclohexanes, and even a little lower than that in 3-methyl-3-phenyl-3-silatetrahydropyran (4.7 kcal/mol),³⁷ apparently due to the less crowded arrangement of substituents (Me,H vs Me,Ph) at the silicon atom.

EXPERIMENTAL SECTION

General Procedures. 3-Methyl-3-*iso*-propoxy-3-silatetrahydropyran was prepared as described earlier.³¹ The organic solvents used were dried and purified according to standard procedures. ¹H, ¹³C, and ²⁹Si NMR spectra were recorded at 400.1 MHz (¹H), 100.6 MHz (¹³C), and 79.5 (²⁹Si) in CDCl₃. Chemical shifts (ppm) were determined relative to internal CHCl₃ (¹H, δ 7.27), internal CDCl₃ (¹³C, δ 77.0), and external TMS (²⁹Si, δ 0.00).

Preparation of 3-Methyl-3-silatetrahydropyran (1). The solution of 3-methyl-3-*iso*-propoxy-3-silatetrahydropyran **5** (2.120 g, 12.3 mmol) in diethyl ether (5 mL) was added dropwise to a stirred suspension of lithium aluminum hydride (0.400 g, 10.5 mmol) in diethyl ether (5 mL) at room temperature. The resulting mixture was heated at reflux for 3 h and was cooled to room temperature. Liquid phase was decanted, and the residue extracted with ether (25 mL). The resulting solid was filtered off. The combined organic phases were added to a stirred mixture of 10% aqueous HCl (15 mL) and *n*-pentane (10 mL). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (2 \times 10 mL). Organic solution was dried over MgSO₄. The solvents were removed by distillation at ambient pressure to give a crude product (1.312 g), which was purified by vacuum distillation to afford **1** (0.722 g, 50% yield, the total yield in four steps in Scheme 2 up to 14%) as a colorless liquid, bp 62 °C/104 mm. ¹H NMR (400 MHz, CDCl₃): δ 0.18 (d, 3H, CH₃–Si, $J = 3.5$ Hz), 0.76 (dddd, 1H, 4-CH^A, $J = 13.5, 8.8, 4.9, \text{ and } 4.4$ Hz), 1.00 (ddd, 1H, 4-CH^B, $J = 13.9, 7.1, \text{ and } 6.7$ Hz), 1.84 (m, 2H, 5-CH₂), 3.44 (dd, 1H, 2-CH^A, $J = 14.7, 3.4$ Hz), 3.55 (m, 2H, 6-CH^A), 3.67 (d, 1H, 2-CH^B, $J = 14.8$ Hz), 3.94 (q, 1H, H–Si, $J = 3.9$ Hz). ¹³C NMR (100 MHz, CDCl₃): δ -7.3 (CH₃–Si), 8.8 (4-CH₂), 25.5 (5-CH₂), 62.1 (2-CH₂), 71.4 (6-CH₂). ²⁹Si NMR (79 MHz, CDCl₃): δ -25.68 ppm. Anal. Calcd. for C₅H₁₂SiO: C, 51.67; H, 10.41. Found: C 51.45; H, 10.11.

GED/MS Measurements. The combined GED/MS experiment was carried out using a technique described earlier.^{43–45} An inlet system constructed from stainless steel, nickel, Teflon, and glass was applied; the vapor flux was regulated by a needle valve. The nozzle temperature during the diffraction patterns exposure was kept at 286(5) K as measured by a W–Re (5/20) thermocouple. The scattered electrons were collected on Kodak Electron Image films ISO 163 of 9 \times 12 cm². Two camera distances, $L_1 = 598$ and $L_2 = 338$ mm, were used resulting in diffraction patterns in the s -range of 1.2 to 14.6 \AA^{-1} and 3.3 to 23.6 \AA^{-1} , respectively ($s = (4\pi/\lambda)\sin(\Theta/2)$), λ is electron wavelength and Θ is scattering angle). The electron wavelengths, 0.04312(5) \AA (L_1) and 0.04260(5) \AA (L_2), were measured from diffraction patterns of polycrystalline ZnO. The diffraction patterns of the gaseous goal compound were recorded with 0.6/1.0 μA primary electron beam intensity, 60/100 s exposure times and a residual pressure of (4.3/3.4) $\times 10^{-6}$ Torr in the diffraction chamber and (2.3/1.0) $\times 10^{-6}$ Torr in the mass spectrometric block for L_1/L_2 camera distances, respectively. The optical densities of the diffraction patterns were measured by a computer controlled microdensitometer.⁴⁶ The molecular scattering function, $sM(s)$, was evaluated as $sM(s) = (I(s)/G(s) - 1)s$ with a step of 0.1 \AA^{-1} , where $I(s)$ is the total electron scattering intensity, and $G(s)$ is the experimental background. Experimental and theoretical $sM(s)$ and radial distribution curves $f(r)$ along with the differences “Experiment–Theory” are given in Figures 2 and 3, respectively.

Least-squares analysis of the scattering intensities was performed using a modified in Ivanovo version of program KCED-35.⁴⁷

Electron impact mass spectrum of 3-methyl-3-silatetrahydropyran recorded at 50 V ionizing voltage showed a molecular peak ($m/z = 116$ a.m.u.) and a set of fragment ions. No ions with the mass heavier than these were detected. The relative intensity of the fragment ions decrease as the ionizing voltage is lowered; at $U_i = 12$ V only a peak of the molecular ion was observed in the mass spectra (see Figure S1 in the Supporting Information).

NMR Measurements. The low temperature ^{13}C NMR spectra were recorded at 150.95 MHz. Standard software was employed for both acquisition (AQ = 0.91 s; relax. delay 2 s; 64K dig. points; power gated; 30° pulse angle -90° : 9.7 μs) and processing (window function: exponential multiplication with 1 Hz line broadening factor). Chemical shifts were determined relative to internal CD_2Cl_2 (^{13}C , δ 53.73 ppm) and are given in ppm downfield to TMS. Assignment of the ^{13}C NMR data was supported by homonuclear (COSY) and heteronuclear (HSQC, HMBC) correlation experiments. The solvent mixture of CD_2Cl_2 , CHFCl_2 , and CH_2Cl_2 in a ratio of 1:1:3 was used for the low temperature measurements. The probe temperature was calibrated by means of a thermocouple inserted into a dummy tube. The low temperature measurements were estimated to be accurate to ± 2 K. The equilibrium constant (K) was determined by integration of the separated signals in the frozen spectrum at 103 K, and the free energy difference was calculated as $\Delta G^\circ = -RT \ln K$. The chemical shifts difference $\Delta\nu[\text{Hz}]$ was determined by extrapolation to the coalescence temperature T_c and used to calculate k_c and the ring inversion barrier by the Eyring equation at T_c .

FTIR Spectroscopy. FTIR spectra of the neat liquid and of the solutions of compound **1** in heptane and methylene chloride were registered in the temperature range 295–83 K in a thermostated cell cooled with liquid nitrogen in 10 cm path cell for gas with KBr windows. The ratio of the 1-ax and 1-eq conformers was calculated from the peak and integral intensities of the components of the doublet $\nu(\text{Si}-\text{H})$ band determined after its graphical separation, assuming equal extinction coefficients of the bands belonging to the axial and equatorial conformers.

■ COMPUTATIONAL DETAILS

Quantum chemical calculations were performed with a Gaussian 09 program suite.⁴⁸ Geometric and vibrational calculations were performed with no restrictions on the geometry by applying DFT and MP2 methods with 6-311G** and cc-pVTZ basis sets.

■ ASSOCIATED CONTENT

● Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02355.

Cartesian coordinates of the calculated structures, details of GED least-squares analysis, FTIR spectra of compound **1** in different states and room-temperature NMR spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: bagrat@irioc.irk.ru (B.A.S.)

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

The financial support of this work by the Russian Foundation for Basic Research (Grant 14-03-00923) is greatly acknowledged.

■ REFERENCES

(1) Bushweller, C. H. *Conformational Behavior of Six-Membered Rings. Analysis, Dynamics, and Stereoelectronic Effects*; Juaristi, E., Ed.; Wiley-VCH: New York, 1995; pp 25–58.

- (2) Kang, F.-A.; Yin, C. L. *J. Am. Chem. Soc.* **1997**, *119*, 8562–8563.
- (3) Cornett, B.; Davis, M.; Wu, S.; Nevins, N.; Snyder, J. P. *J. Am. Chem. Soc.* **1998**, *120*, 12145–12146.
- (4) Oliveira, P. R.; Rittner, R. *Spectrochim. Acta, Part A* **2005**, *61*, 1737–1745.
- (5) Oliveira, P. R.; Ribeiro, D. S.; Rittner, R. *J. Phys. Org. Chem.* **2005**, *18*, 513–521.
- (6) Kleinpeter, E.; Taddei, F.; Wacker, P. *Chem. - Eur. J.* **2003**, *9*, 1360–1368.
- (7) Kirby, A. J. *The Anomeric Effects and Related Stereoelectronic Effects at Oxygen*; Springer Verlag: Berlin, 1983; pp 50–52.
- (8) Alabugin, I. V.; Manoharan, M.; Zeidan, T. A. *J. Am. Chem. Soc.* **2003**, *125*, 14014–14031.
- (9) Ribeiro, D. S.; Rittner, R. *J. Org. Chem.* **2003**, *68*, 6780–6787.
- (10) Wiberg, K. B.; Hammer, D. J.; Castejon, H.; Bailey, W. F.; DeLeon, E. L.; Jarret, R. M. *J. Org. Chem.* **1999**, *64*, 2085–2095.
- (11) Eliel, E. L.; Hargrave, K. D.; Pietrusiewicz, K. M.; Manoharan, M. *J. Am. Chem. Soc.* **1982**, *104*, 3635–3643.
- (12) Willer, R. L.; Eliel, E. L. *J. Am. Chem. Soc.* **1977**, *99*, 1925–1936.
- (13) Eliel, E. L.; Kandasamy, D.; Yen, C.; Hargrave, K. D. *J. Am. Chem. Soc.* **1980**, *102*, 3698–3707.
- (14) Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; pp 24–42 and 743.
- (15) Kleinpeter, E.; Thielemann, J. *Tetrahedron* **2007**, *63*, 9071–9081.
- (16) Kleinpeter, E.; Heydenreich, M.; Koch, A.; Linker, T. *Tetrahedron* **2012**, *68*, 2363–2373.
- (17) Bodi, A.; Kvaran, A.; Jonsdottir, S.; Antonsson, E.; Wallevik, S. Ó.; Arnason, I.; Belyakov, A. V.; Baskakov, A. A.; Hölbling, M.; Oberhammer, H. *Organometallics* **2007**, *26*, 6544–6550.
- (18) Wallevik, S. O.; Bjornsson, R.; Kvaran, A.; Jonsdottir, S.; Arnason, I.; Belyakov, A. V.; Kern, T.; Hassler, K. *Organometallics* **2013**, *32*, 6996–7005.
- (19) Klaeboe, P.; Aleksa, V.; Nielsen, C. J.; Horn, A.; Guirgis, G. A.; Johnston, M. D. *J. Mol. Struct.* **2012**, *1015*, 120–128.
- (20) Girichev, G. V.; Gricheva, N. I.; Bodi, A.; Gudnason, P. I.; Jonsdottir, S.; Kvaran, A. I.; Arnason, I.; Oberhammer, H. *Chem.—Eur. J.* **2007**, *13*, 1776–1783.
- (21) Kern, T.; Hölbling, M.; Dzambaski, A.; Flock, M.; Hassler, K.; Wallevik, S. Ó.; Arnason, I.; Bjornsson, R. *J. Raman Spectrosc.* **2012**, *43*, 1337–1342.
- (22) Wallevik, S. O.; Bjornsson, R.; Kvaran, A.; Jonsdottir, S.; Arnason, I.; Belyakov, A. V.; Baskakov, A. A.; Hassler, K.; Oberhammer, H. *J. Phys. Chem. A* **2010**, *114*, 2127–2135.
- (23) Arnason, I.; Kvaran, A.; Jonsdottir, S.; Gudnason, P. I.; Oberhammer, H. *J. Org. Chem.* **2002**, *67*, 3827–3831.
- (24) Belyakov, A. V.; Sigolaev, Y.; Shlykov, S. A.; Wallevik, S. O.; Jonsdottir, N. R.; Bjornsson, R.; Jonsdottir, S.; Kvaran, A.; Kern, T.; Hassler, K.; Arnason, I. *Struct. Chem.* **2015**, *26*, 445–453.
- (25) Shainyan, B. A.; Kirpichenko, S. V.; Osadchiy, D. Yu.; Shlykov, S. A. *Struct. Chem.* **2014**, *25*, 1677–1685.
- (26) Shainyan, B. A.; Kleinpeter, E. *Tetrahedron* **2012**, *68*, 114–125.
- (27) Shainyan, B. A.; Kirpichenko, S. V.; Kleinpeter, E.; Shlykov, S. A.; Osadchiy, D.; Yu; Chipanina, N. N.; Oznobikhina, L. P. *J. Org. Chem.* **2013**, *78*, 3939–3947.
- (28) Kirpichenko, S. V.; Kleinpeter, E.; Ushakov, I. A.; Shainyan, B. A. *J. Phys. Org. Chem.* **2011**, *24*, 320–326.
- (29) Shlykov, S. A.; Osadchiy, D.; Yu; Chipanina, N. N.; Oznobikhina, L. P.; Shainyan, B. A. *J. Mol. Struct.* **2015**, *1100*, 555–561.
- (30) Weldon, A. J.; Tschumper, G. S. *Int. J. Quantum Chem.* **2007**, *107*, 2261–2265.
- (31) Kirpichenko, S. V.; Shainyan, B. A. *Tetrahedron* **2015**, *71*, 599–604.
- (32) Sipachev, V. A. *J. Mol. Struct.* **2001**, *567–568*, 67–72.
- (33) Sipachev, V. A. *J. Mol. Struct.: THEOCHEM* **1985**, *121*, 143–151.
- (34) Hamilton, W. C. *Acta Crystallogr.* **1965**, *18*, 502–510.

- (35) Favero, L. B.; Velino, B.; Caminati, W.; Arnason, I.; Kvaran, A. *Organometallics* **2006**, *25*, 3813–3816.
- (36) Carleer, R.; Anteunis, M. J. O. *Org. Magn. Reson.* **1979**, *12*, 673–678.
- (37) Shainyan, B. A.; Kirpichenko, S. V.; Kleinpeter, E.; Shlykov, S. A.; Osadchiy, D. Yu. *Tetrahedron* **2015**, *71*, 3810–3818.
- (38) Breed, H. E.; Gundersen, G.; Seip, R. *Acta Chem. Scand.* **1979**, *33*, 225–233.
- (39) Anet, F. A. L.; Bradley, C. H.; Buchanan, G. W. *J. Am. Chem. Soc.* **1971**, *93*, 258–259.
- (40) Pihlaja, K.; Kleinpeter, E. Conformational and Configurational Analysis and Substituents Effects on the ¹³C NMR Chemical Shifts of Alicyclic Compounds. In *Carbon-13 NMR Chemical Shifts in Structural and Stereochemical Analysis*; VCH Publisher, Inc.: New York, 1994; Chapter 4A, pp 79–156.
- (41) Shainyan, B. A.; Kleinpeter, E. *Tetrahedron* **2013**, *69*, 5927–5936.
- (42) Lambert, J. B.; Mixan, C. E.; Johnson, D. H. *J. Am. Chem. Soc.* **1973**, *95*, 4634–4639.
- (43) Girichev, G. V.; Utkin, A. N.; Revichev, Yu. F. *Instrum. Exp. Techn.* **1984**, *27*, 457–461.
- (44) Girichev, G. V.; Shlykov, S. A.; Petrova, V. N.; Subbotina, N. Y.; Lapshina, S. B.; Danilova, T. G. *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol.* **1988**, *31*, 46–51 (in Russian).
- (45) Girichev, G. V.; Shlykov, S. A.; Revichev, Y. F. *Prib. Tekh. Eksp.* **1986**, *4*, 167–169 (in Russian).
- (46) Girichev, E. G.; Zakharov, A. V.; Girichev, G. V.; Bazanov, M. I. *Izv. Vyssh. Uchebn. Zaved. Tekhnol. Tekst. Prom.* **2000**, *2*, 142–146 (in Russian).
- (47) Andersen, B.; Seip, H. M.; Strand, T. G.; Stølevik, R. *Acta Chem. Scand.* **1969**, *23*, 3224–3234.
- (48) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery Jr., J. A.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, O.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09* revision C.01.; Gaussian, Inc.: Wallingford CT, 2009.