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SYNTHESIS AND CONFORMATION OF SOME 2,4-DIOXA- AND 2,4-DIOXA-3-SILABICYCLO[3.3.1]NONANES

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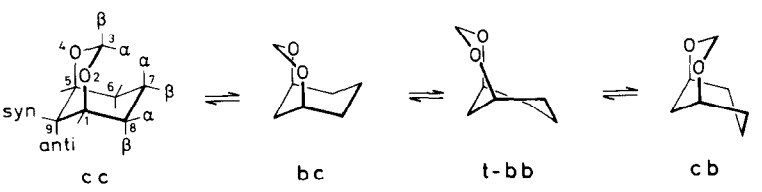
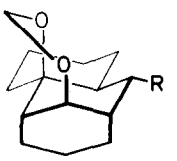
Abstract—The conformation of the title compounds established by ^{13}C and ^{1}H NMR spectroscopy shows that replacement of the 2- and 4-methylene groups in bicyclo[3.3.1]nonane by ether oxygen atoms strongly destabilizes the **cc** conformation: in 2-oxabicyclo[3.3.1]-nonane the **cc** and the **bc** conformers are about equally populated, whereas in 2,4-dioxabicyclo[3.3.1]nonane the **bc** conformation predominates. The 2,4-dioxa-3-silabicyclo[3.3.1]nonanes also occur predominantly in the **bc** conformation. As in the carbocyclic bicyclo[3.3.1]nonanes both wings are strongly flattened. A stereoselective synthesis of 3α-methylbicyclo[3.3.1]nonane, an important model compound in this study, is described.

It has been shown that bicyclo[3.3.1]nonane exists predominantly in the chair–chair conformation (**cc**).[1,2] It is now well established that the energy difference between this conformation and the boat-chair conformation (**bc**) is 10.5 kJ mol^{-1}.[3] The **bc** conformation is in turn 22.6 kJ mol^{-1} more stable than the double twist boats (**t-bb**).[2] In all conformations severe non-bonding interactions occur between both wings, consequently the wings are strongly flattened. With the introduction of lanthanide shift reagents and of high field spectrometers, ^{1}H and ^{13}C NMR spectroscopy have become valuable tools in the conformational analysis of bicyclo[3.3.1]nonanes in solution.[2] It may be expected that the replacement of the 2- and 4-methylene units by ether oxygens will change the interactions, which contribute to the conformational features of these systems. The most profound alteration is the increase of the interaction of the CH_2 at the 3-position and the cyclohexane ring in the **cc**, the **bc** and the **cb** conformations, because of the shorter C–O bonds in the oxa compounds. Previously, with the use of molecular mechanics, we have computed that the introduction of 2- and 4-ether oxygens causes a destabilization of the **cc** with respect to the **bc** conformation.[4] In 2-oxabicyclo[3.3.1]nonane (**2**) the **cc** and the **bc** are computed to be about equally strained, whereas for 2,4-dioxabicyclo[3.3.1]nonane (**3**) the calculated steric strain of the **cc** is 8.3 kJ mol^{-1} higher than that of the **bc** conformation. The NMR techniques, used for the conformational analysis of the carbocyclic systems can also be applied to the cyclohexane wing of dioxabicyclo[3.3.1]nonanes, but it is rather difficult to obtain information on the geometry of the dioxane wing, due to the absence of vicinal H–H couplings in the $C_1OC_3OC_5$ part. Only a few studies on the conformation of 2,4-dioxabicyclo[3.3.1]nonanes have been published. Marvell and Provant described one of the epimers of 3-methyl-2,4-dioxabicyclo[3.3.1]nonane and demonstrated that the cyclohexane part of this compound is predominantly in the chair form;[5] the configuration and the conformation of the dioxane ring, however, were not established. Anteunis *et al.* have studied the conformation of 2,4-dioxabicyclo[3.3.1]nonane (**3**) and of its 7,7-dimethyl derivative using several ^{1}H NMR techniques.[6,7] Although it was assumed that these compounds exist in a flattened **cc** or **t-bb**, no definitive conclusions were possible. Based on dipole moment measurements, Bishop *et al.* concluded that the 2,4-dioxabicyclo[3.3.1]nonane part in compound **1** adopts th **bc** conformation.[8]





R = C_6H_5
p-Cl-C_6H_4
p-NO_2-C_6H_4

1

The present investigation deals with a conformational analysis of 2-oxabicyclo[3.3.1]nonane (**2**), 2,4-dioxabicyclo[3.3.1]nonane (**3**), some of its methyl derivatives (**4–6**) and some 2,4-dioxa-3-silabicyclo[3.3.1]nonanes (**7–9**) with the use of ^{13}C and ^{1}H NMR spectroscopy.

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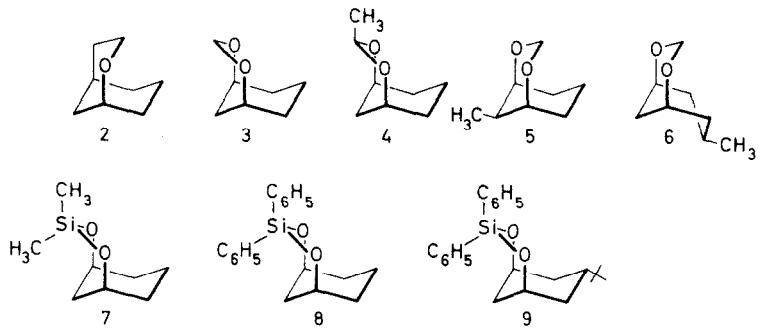


From the previous empirical force field calculations it can be concluded that compound **4** strongly prefers the **bc** conformation, whereas for compound **5** it may be safely assumed that the dioxane wing prefers the chair conformation.[4] Therefore, these compounds were used as model compounds for a system with a boat and chair dioxane wing, respectively. In order to establish the configuration of **4** a stereoselective synthetic route towards this compound was developed.

RESULTS AND DISCUSSION

2-oxabicyclo[3.3.1]nonane (**2**) was synthesized starting from 3-hydroxyphenylacetic acid (**10**). Hydrogenation in alkaline medium with Rh/C as the catalyst gave a *cis/trans* mixture of the corresponding cyclohexane derivative (**11**) (Scheme 1). After esterification with diazomethane and reduction with LAH a *cis/trans* mixture of 3-hydroxycyclohexylethanol (**12**) was obtained. Reaction with 1 equivalent of methanesulfonyl chloride afforded the mono mesylate **13**, which was cyclized in low yield to 2-oxabicyclo[3.3.1]nonane, with the use of NaH in DMSO.

The 2,4-dioxabicyclo[3.3.1]nonanes **3–6** were synthesized by pyrolysis of the mixed acetals of the corresponding cyclohexane-1,3-diols, ethanol and the appropriate aldehyde, according to the procedure described by Anteunis *et al.*[11] It should be noted that a *cis/trans* mixture of the cyclohexane-1,3-diols is suitable for the reaction: only the *cis* isomer gives volatile products. From cyclohexane-1,3-diol, ethanol and acetaldehyde one of the isomers of 3-methyl-2,4-dioxabicyclo[3.3.1]nonane (>99%) was obtained. As this procedure may give a kinetically determined product,[11] a direct acetalization of cyclohexane-1,3-diol with acetaldehyde under equilibrium conditions, using silica–alumina as the catalyst, was also performed.[12] The same compound again was the main product. Only a very small amount (<1%) of an isomer could be detected. In order to establish the configuration of the 3-methyl-2,4-dioxabicyclo[3.3.1]nonane obtained, a selective route for the 3α-methyl epimer **4** was developed. An attractive starting compound was 3α-methanesulfonoxymethyl-2,4-dioxabicyclo[3.3.1]non-6-ene (**19**), the synthesis of which has been described by Woodward.[13] Since this synthesis proceeds *via* 2-oxo-3,7,8-trioxatricyclo[4.3.1.1^{4,9}]undecane (**16**) (Scheme 2), the 3α-epimer is obtained exclusively. Hydrogenation of **19** with Pt/C as the catalyst gave the corresponding saturated dioxabicyclo[3.3.1]nonane **20**. During the synthetic route up to that stage some hydrolysis of the mesylate had occurred. Therefore, the mixture obtained was treated with mesyl chloride to yield the mesylate **20** as the sole product. Reduction with LAH gave the desired 3α-methyl-2,4-dioxabicyclo[3.3.1]nonane (**4**). The compound obtained was identical with that obtained from the acetalization reactions. The analogy between the ^{13}C chemical shifts of compounds **17**, **18**, **20** and **4** (see Table 1) indicates that no epimerization has occurred during this synthesis Moreover, under the conditions applied for the hydrogenation of **19**, it was observed that *r*-2-methyl-4-*trans*-methyl-6-*trans*-methyl-1,3-dioxane[14] did not epimerize to the thermodynamically more stable all-*cis* compound.

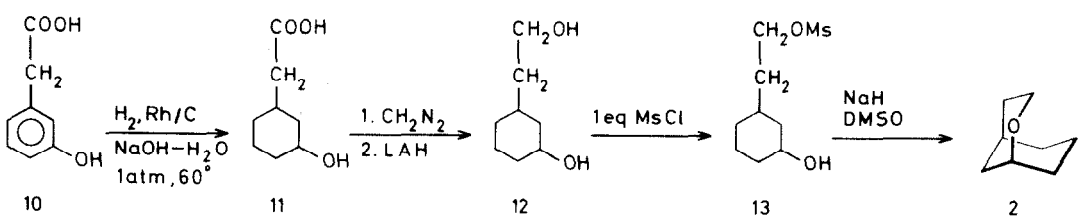
Upon treatment of 3α-methyl-2,4-dioxabicyclo[3.3.1]nonane (**4**) with $BF_3.OEt_2$, initially a small amount of an isomer (probably the 3β-methyl epimer) was formed. However, on prolonged reaction a complex mixture of unidentified products was obtained.

The almost exclusive formation of the 3α-methyl epimer during the acetalization reactions is in agreement with the computed high stability of this compound with respect to its 3β-methyl epimer.[4] The calculated difference in steric strain of these compounds is 9.5 kJ mol^{-1}. It seems most likely that the compound described by Marvell and Provant[5] is also **4**.

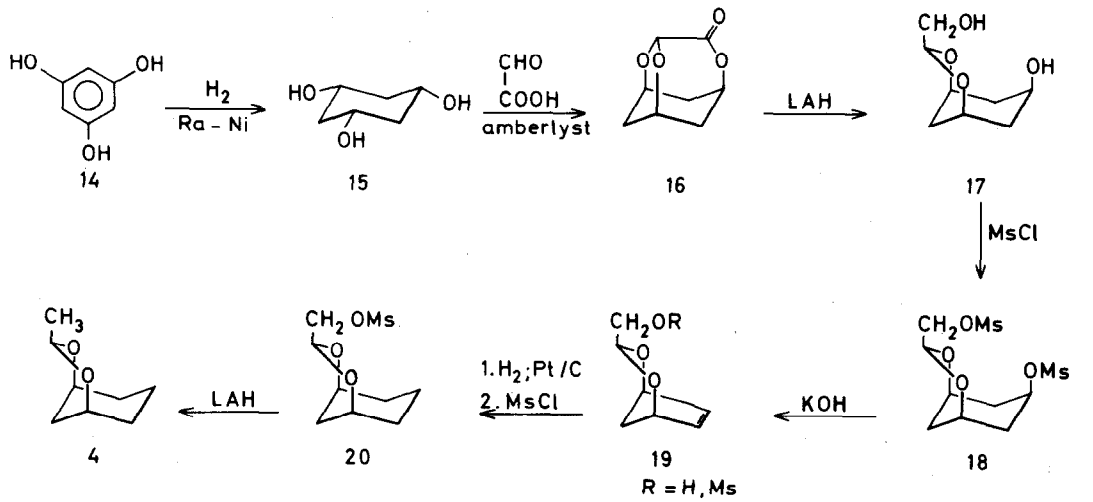
The 2,4-dioxa-3-silabicyclo[3.3.1]nonanes **7–9** were synthesized from cyclohexane-1,3-diols and dimethyl or diphenyldichlorosilane, according to the procedure of Krieble and Burkhard.[15]

^{13}C NMR spectroscopy

The ^{13}C chemical shifts of the compounds studied are compiled in Table 1. Peak assignments were made with



Scheme 1.



Scheme 2.

the use of the off-resonance technique, the relative intensities, and intercomparison of the chemical shifts taking into account substituent effects.

In order to reveal conformational factors in the ^{13}C chemical shifts, it is primarily necessary to correct for the influence of the 3-, 7- and 9-substituents. Previously, for the carbocyclic analogues, it was shown that good estimates for substituent effects can be obtained from the corresponding monocyclic compounds.[16] Therefore, the substituent effects in the 2,4-dioxabicyclo[3.3.1]nonanes were estimated from the substituent effects in the carbocyclic analogues,[16] cyclohexane and dioxanes.[17-19] For compounds **3–6** the ^{13}C chemical shifts corrected in this way are given in Table 2. It can be seen that the conformational effects observed in the carbocyclic bicyclo[3.3.1]nonanes[16] and in 3-oxabicyclo[3.3.1]nonanes[4] are also present in the compounds of the present study. The corrected chemical shifts of C_6, C_7 and C_9 of compounds **4** and **6** are close to those of the carbocyclic analogues. From the relatively upfield corrected chemical shift of C_6 of compound **6**, it can be concluded that in that compound the **cb** conformation predominates. In the chemical shifts of C_3 of **3–6** the same trends are observed as for the carbocyclic analogues, where the differences are due to the deshielding effect of the ether oxygens. It may be noted that the conformational influences on ^{13}C chemical shifts for bicyclo[3.3.1]nonanes, 3-oxabicyclo[3.3.1]nonanes and 2,4-dioxabicyclo[3.3.1]nonanes are about the same. Apparently the steric effects of the ether oxygen atoms on

Table 1. ^{13}C chemical shifts of 2,4-dioxabicyclo[3.3.1]nonanes and 3-sila-2,4-dioxabicyclo[3.3.1]nonanes.

Compound	^{13}C chemical shifts (δ ± 0.1 ppm)					
nr	C_1	C_3	C_6	C_7	C_9	substituents
3	67.9	84.5	32.4	15.9	27.3	
4	68.4	88.6	32.6	15.9	27.7	21.2
5	71.9	86.8	31.1	17.9	34.7	19.0
6	66.7	81.4	34.9	23.3	28.8	21.8
7	68.5	--	32.6	15.4	36.1	0.7; 3.0
8	69.4	--	32.4	15.5	36.3	127.4; 129.5; 129.9; 134.1
9	70.4	--	33.7	35.8	36.6	127.5; 129.8; 130.0; 134.3
17	67.6	90.4	39.1	64.6	26.1	61.9
18	65.7	88.3	36.3	75.6	25.2	70.2; 37.8; 36.8
20	68.7	88.4	32.1	15.7	27.7	70.3

Table 2. Corrected ^{13}C chemical shifts of 2,4-dioxabicyclo[3.3.1]nonanes

Compound	Corrected ^{13}C chemical shifts (± 0.1 ppm)				
nr	C_1	C_3	C_6	C_7	C_9
3	67.9	84.5	32.4	15.9	27.3
4	68.7	83.5	32.6	15.9	27.7
5	66.8	86.5	30.4	17.9	31.4
6	66.0	81.4	25.7	17.7	28.8

the chemical shifts are about the same as those of CH_2 groups. A comparison of the corrected ^{13}C shifts of compounds **3** and **4** domonstrates that 2,4-dioxabicyclo[3.3.1]nonane (**3**) is predominantly in the **bc** conformation. The corrected ^{13}C chemical shifts of compound **5** are between those expected for **cc** and **cb** conformations, suggesting that this compound exists as a **cc–bc** mixture. This is confirmed by relatively large and non-linear temperature dependences of the ^{13}C chemical shifts of this compound (in particular those of C_3, C_6, C_7 and the Me group; 0.008 ppm/°C). For conformationally homogeneous bicyclo[3.3.1]nonanes these temperature effects are linear and small (0.004 ppm/°C).[2] From these temperature dependences, using the procedure described previously,[2] the enthalpy difference between **cc** and **bc** conformations of **5** is estimated to be about 6 kJ mol.$^{-1}$ Taking into account the crudeness of this estimation, this is in rather good agreement with the value obtained from force field calculations (2.4 kJ mol^{-1}).[4]

The ^{13}C chemical shifts of C_6, C_7 and C_9 of compound **20** (see Table 1) shows it to be predominantly in the **bc** conformation. The corresponding shifts in compounds **17** and **18** are influenced by substituent effects, but comparison of the chemical shifts in the dioxane ring shows that compound **18** is also predominantly **bc**, whereas **17** might be partly **cc**.

The ^{13}C chemical shifts of C_6 and C_7 of the 3-sila-2,4-dioxabicyclo-[3.3.1]nonanes **7–9** (see Table 1) show that these compounds also prefer the **bc** conformation. The downfield chemical shifts of C_9 might be ascribed to the high steric compression, which must be present in the boat wing of these compounds.

Unfortunately, the substituent effects of hetero-atoms in cyclic compounds are rather sensitive to both the position of that hetero-atom and conformational effects.[18,19] Therefore, a direct comparison between the oxabicyclo[3.3.1]nonanes and the corresponding carbocyclic compounds often is not accurate. For the interpretation of the ^{13}C chemical shifts of 2-oxabicyclo[3.3.1]nonane (**2**), however, we have to rely on such a comparison, since no related compounds in the 2-oxa series were available. With the use of hetero-O atom substituent effects, estimated from ^{13}C chemical shifts in 3-oxabicyclo[3.3.1]nonane,[20] 9-oxabicyclo[3.3.1]nonane, tetrahydropyran, and 2-oxa-adamantane[19] rough estimates were made for the ^{13}C chemical shifts of **cc** and **bc** conformations of compound **2** (see Table 3). A comparison with the experimental values shows that **2** probably contains substantial amounts of both conformers.

^1H NMR spectroscopy

^1H NMR spectra (60–100 MHz) of compounds **2–10** were recorded with increasing amounts of Eu(dpm)$_3$ or Eu(fod)$_3$ until optimal separation between the various multiplets was achieved. The signals were assigned by the splitting patterns, double resonance techniques and by the magnitudes of the lanthanide induced shifts. The expanded spectra allowed first-order analysis of the most significant vicinal couplings. The coupling constants obtained were independent of the amount of shift

Table 3. Estimated and experimental ^{13}C chemical shifts of 2-oxabicyclo[3.3.1]nonane (**2**)

atom	calculated		experimental
nr	cc	bc	
1	67.2-69.8	65.0-67.6	67.9
3	63.7-64.0	60.4-60.7	61.3
4	31.1	26.3	30.5[a]
5	24.6-27.5	22.4-25.3	24.3
6	30.4-31.5	32.2-33.0	31.2[a]
7	21.8-22.3	15.9-16.4	19.3
8	30.4-31.5	32.2-33.0	31.6[a]
9	32.6-34.0	26.8-28.2	31.9[a]

[a] These chemical shifts may be interchanged.

Table 4. Vicinal proton-proton coupling constants $J_{18\beta}$ of compounds **2–9** (Hz ± 0.5)

2	3	4	5	6	7	8	9
2.5	0.7	< 2	3.5	8.0	< 2	< 2	< 2

reagent added, showing that the shift reagent has no significant influence on the geometry and the conformational equilibria. Sometimes line broadening hampered an accurate determination of the coupling constants.

In particular the coupling constant $J_{18\beta}$ is diagnostic for the conformation of the cyclohexane wing of the systems studied. These couplings are compiled in Table 4.

The coupling $J_{18\beta}$ for compounds **2–4** and **7–9** is small, which is characteristic for a chair conformation of the wing under consideration, whereas the high value of $J_{18\beta}$ of compound **6** shows that the cyclohexane wing in **6** is predominantly in the boat conformation.[21] With the use of the semi-empirical relationship of Altona *et al.*[22,23] and the dihedral angles obtained by molecular mechanics,[4] the coupling constants $J_{18\beta}$ for **3 bc** and **6 cb** can be calculated to be 1.7 and 9.0 ppm, respectively.

The value of $J_{18\beta}$ for compound **5** indicates contributions of both the chair and the boat conformation for the cyclohexane wing, which is in agreement with the conclusions of ^{13}C NMR studies.

Information on the geometry of the dioxane wing cannot be obtained from the vicinal proton-proton coupling constants. For all compounds, with the exception of 2,4-dioxabicyclo[3.3.1]nonane (**3**), the conformation of this ring can be deduced from the conformation of the cyclohexane part of the system by elimination of conformations involving extreme 3,7- or 3,9-interactions. Thus **4**, **7–9** are predominantly in the **bc** conformation, **6** is **cb**, **5** exists as a **cc**, **cb** mixture and **2** as a **bc**, **cc** mixture. The latter is confirmed by the couplings between $H_{3\alpha}/H_{3\beta}$ and $H_{4\alpha}/H_{4\beta}$, which are all about 7 Hz. Moreover, in **2** $J_{54\beta}$ is 6–7 Hz. The magnitudes of these coupling constants indicate that the **bc** and the **cc** are about equally populated.[21]

As already reported in a preliminary communication,[10] the conformation of **3** can be investigated with the use of Nuclear Overhauser Effects and T_1 relaxation times. Upon saturation of the H_3 signal at $\delta = 4.79$ only a NOE on the H_3 signal at $\delta = 5.04$ could be detected, whereas saturation of H_{9syn} induces significant NOE's on H_{9anti} and the H_3 signal at $\delta = 5.04$. Thus, it could be concluded that **3** occurs predominantly in the **bc** conformation. Moreover, it was possible to assign the signals at $\delta = 5.04$ and 4.79 to $H_{3\beta}$ and $H_{3\alpha}$, respectively. These conclusions were confirmed by comparison of calculated and experimental T_1 relaxation times.[10]

In order to get a more detailed picture of the geometry of 2,4-dioxabicyclo[3.3.1]nonane (**3**) accurate values of all proton-proton coupling constants were subtracted from the 300 MHz ^1H NMR spectrum (Table 5).The signals were assigned by the splitting patterns and by taking into account the $Eu(dpm)_3$ induced shifts. In this way we arrived at different assignment than that of Anteunis *et al.*,[9,10] but the magnitudes of the coupling constants agreed well with the couplings obtained by these authors.

With the use of the relationship of Altona *et al.*[22,23] from the vicinal coupling constants the various dihedral angles were estimated. In Table 6 these angles are compared with those obtained from force field calculations.[4] It can be seen that the agreement is rather good and it may be inferred that the cyclohexane part of the 2,4-dioxabicyclo[3.3.1]nonane system is strongly flattened.

CONCLUSIONS

Replacement of the 2- and 4-CH_2 groups in bicyclo[3.3.1]nonane strongly destabilizes the **cc** conformation. In 2-oxabicyclo[3.3.1]nonane, **cc** and **bc** conformations are about equally populated, whereas 2,4-dioxabicyclo[3.3.1]nonane exists predominantly in the **bc** conformation. The cyclohexane wing of the system is strongly flattened. Previous force field calculations have shown that this is also the case with the other wing. Substitution at the 9-syn position by a Me group gives rise to destabilization of **bc**: then **cc** and **cb** are favoured. The results of the present NMR study are in excellent agreement with those of previous force field calculations.[4]

The conformational features of the 3-sila-2,4-dioxabicyclo[3.3.1]nonanes are analogous to those of the 2,4-dioxabicyclo[3.3.1]nonanes. Although the sila compounds studied all have bulky substituents at both the 3α and the 3β position, **bc** is the preferred conformation. As a result of the larger Si–O and Si–C bond lengths com-

Table 5. Chemical shifts (ppm ± 0.01) and coupling constants (Hz ± 0.2) in compound **3** (1.4 mole % in C_6D_6, degassed)

1	3α	3β	6α	6β	7α	7β	9syn	9anti
4.05	4.79	5.04	1.83	0.95	2.45	1.28	2.08	0.70

$J_{18\alpha}$	$J_{18\beta}$	J_{19syn}	J_{19anti}	$J_{6\alpha7\alpha}$	$J_{6\alpha7\beta}$	$J_{6\beta7\alpha}$	$J_{6\beta7\beta}$
4.9	1.5	5.0	1.0	4.8	2.1	13.1	5.2

$J_{9syn6\alpha}$	$J_{3\alpha3\beta}$	$J_{6\alpha6\beta}$	$J_{7\alpha7\beta}$	$J_{9syn9anti}$
2.4	-5.5	-13.4	-13.7	-14.4

Table 6. Comparison of dihedral angles in 3 estimated from coupling constants with those obtained from molecular mechanics (degrees)

	estimated from coupling constant	obtained from molecular mechanics
18α	54.7	57.7
19syn	54.1	49.8
6,7α	-50.8	-51.1
6,7β	65.4	64.4
6,7α	-163.4	-168.4
6,7β	-49.1	-53.0

pared with C–O and C–C, the interaction between the 3β-substituent and H_{9syn} in these compounds should be less severe than in the carbon analogues.

EXPERIMENTAL

The 60 MHz ^{1}H NMR spectra were recorded on a Varian T-60 apparatus, 100 MHz ^{1}H NMR spectra on a Varian XL-100-15 spectrometer in the FT mode, and 300 MHz ^{1}H NMR spectra on a spectrometer built at the Department of Applied Physics.[24] ^{13}C NMR spectra were measured at a Varian CFT-20 (20 MHz) or at the Varian XL-100-15 spectrometer in the FT mode (25 MHz). Mass spectra were recorded by Messrs B. van de Graaf, P. J. W. Schuyl and Mrs A. H. Knol-Kalkman on a Varian-MAT 311A mass spectrometer.

Eu(dpm)$_3$ was obtained from Merck, Eu(fod)$_3$ was synthesized according to the procedure of Sievers *et al*[25,26] The shift reagents were sublimed at 180°/0.1 mm and after that handled in a glove box, flushed with dry nitrogen. The solvents used in LIS experiments were dried on Zeolite KA prior to use.

3-hydroxycyclohexylacetic acid (**11**). A soln of 3-hydroxyphenylacetic acid (22.0 g, 0.15 mole) in 600 ml of aq 0.4 M NaOH was hydrogenated at 1 atm and 60° with 10 g 5% Rh/C as the catalyst. After 3 h the hydrogen-uptake ceased. The catalyst was filtered off, the filtrate was saturated with NaCl, and then acidified with H_2SO_4 until pH 1. The dispersion obtained was extracted with EtOAc (4 × 150 ml). The organic layers were dried over $MgSO_4$ and after that the solvents were evaporated to yield 22.5 g of compound **11** (0.14 mole, 99%).

Methyl 3-hydroxycyclohexylacetate. The product of the preceding step was esterified with an excess of CH_2N_2 in diethyl ether. After evaporation of the excess of reagent and of the solvent 21.6 g methyl 3-hydroxycyclohexylacetate (0.13 mole, 92%) was obtained; ^{1}H NMR (60 MHz, CD_3OD) δ 4.6 (1 H, s), 3.9 (1 H, m), 3.6 (3 H, s) 1.0–2.1 (11 H); mass spectrum (70 eV): characteristic peaks at *m/z* 154, 141, 129.

2-(3-hydroxycyclohexyl)ethanol (**12**). The product of the preceding step was dissolved in 115 ml dry THF and added dropwise to a suspension of 4.8 g LAH (0.13 mole) in 150 ml dry THF. The mixture was boiled for 3 h. After cooling 10 ml H_2O and then 200 ml 4N H_2SO_4 were added dropwise. The aqueous layer was extracted with EtOAc (5 × 100 ml). The combined organic layers were washed with sat. NaCl aq. (2 × 150 ml) and dried over $MgSO_4$–K_2CO_3. After evaporation of the solvents 17.2 g of **12** (0.12 mole, 95%) was obtained; ^{1}H NMR (60 MHz, $CDCl_3$): δ 2.9–4.0 (5 H), 0.8–2.1 (11 H); ^{13}C NMR (20 MHz, $CDCl_3$): δ 70.5, 66.5, 60.0, 59.9, 39.8, 39.3, 39.0, 35.6, 33.2, 32.7, 32.3, 27.9, 24.2, 20.2.

Monomesylate of 2-(3-hydroxycyclohexyl)ethanol (**13**). A soln of 25.7 g of **12** (0.19 mole) in 400 ml dry pyridine was cooled to 0°. Then 14.4 ml mesyl chloride (0.18 mole) was added with rapid stirring. The mixture was stored at 0° for 18 h. After that it was poured onto 960 ml of 1N HCl (0°). The precipitate was filtered off to yield 6.6 g of the dimesylate. The filtrate was saturated with NaCl and extracted with EtOAc (5 × 125 ml). The EtOAc soln was washed with sat. NaCl aq. (2 × 150 ml) and dried over $MgSO_4$. Evaporation of the solvents gave 25 g monomesylate **13** (0.11 mole, 63%); ^{1}H NMR (60 MHz, $CDCl_3$): δ 4.3 (2 H, t, *J* = 6.5 Hz), 3.9 (2 H, m), 3.0 (3 H, s), 1.0–2.1 (11 H).

2-oxabicyclo[3.3.1]nonane (**2**). NaH (1.15 g, 50% dispersion in paraffin, 23 mmole) was stirred with 25 ml light petroleum for 15 min in a N_2 atmosphere. The solvent was decanted and then 30 ml of DMSO was added to the NaH. To this dispersion a soln of 5.55 g of **13** (25 mmole) in 30 ml DMSO was added dropwise. The reaction mixture was stirred at 70° for 20 h. After cooling 20 ml H_2O was added and then the mixture obtained was extracted with diethyl ether (5 × 20 ml). The organic layers were washed with H_2O (3 × 35 ml) and dried over $MgSO_4$. After that most of the solvent was distilled off. The residue was purified by chromatography over alumina (elution with light petroleum). From the eluate the solvents were distilled off and the residue was distilled under reduced pressure to yield 124.9 mg pure **2** (0.99 mmole, 4%); b.p. 69°/13 mm; ^{1}H NMR (60 MHz, $CDCl_3$): δ 3.7–4.2 (3 H), 1.6–2.4.

2,4-dioxabicyclo[3.3.1]nonane (**3**).[11] A mixture of 300 ml of C_6H_6, 50 ml EtOH and 11.7 g of cyclohexane-1,3-diol (0.1 mole, about 40% *cis* and 60% *trans*), 9 g paraformaldehyde (0.3 mole) and some crystals *p*-TsOH were boiled for 1.5 h. The H_2O formed was removed by azeotropic distillation. Then the solvents were evaporated under vacuo. The residue was pyrolized at 10 mm Hg. The product was redistilled to yield 3.4 g pure **3** (26.6 mmole, 40%); b.p. 71–72°/17 mm; m.p. 36–39°; mass spectrum: important peaks at *m/z* 128, 127, 97, 85, 83, 81.

3α-methyl-2,4-dioxabicyclo[3.3.1]nonane (**4**) *starting from cyclohexane-1,3-diol.* Analogous to the procedure described in the previous section, with acetaldehyde as starting material, **4** was obtained with a yield of 24%; b.p. 77–83°/17 mm; ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.3 (1 H, q, *J* = 4.5 Hz), 4.3 (2 H, m), 1.0–2.9 (11 H); mass spectrum (70 eV): important peaks at *m/z* 142, 141, 127, 81. Somewhat better results were obtained by a direct acetalization of cyclohexane-1,3-diol with acetaldehyde and the silica–alumina HA-LPV (obtained from Akzo-Amsterdam) in the presence of Zeolite KA as the catalyst. A mixture of 2.5 g cyclohexane-1,3-diol (22.7 mmole, *cis*:*trans* = 2:1), 25 ml $CHCl_3$, 1 g freshly distilled acetaldehyde, 5 g KA powder (activated at 400°) and 1 g HA-LPV (activated at 400°) were stirred at room temp. for 20 h. Then the mixture was filtered. From the filtrate the solvents were evaporated. After that the residue was distilled under reduced pressure to yield 720 mg pure **4** (5.1 mmole, 34%). This compound was identical to that obtained by the procedure described above.

3α-methanesulfonoxymethyl-2,4-dioxabicyclo[3.3.1]nonane (**20**). 3α-methanesulfonoxymethyl-2,4-dioxabicyclo[3.3.1]non-6-ene (**19**)[13] (12.8 g, contaminated with about 30% of the corresponding 3α-hydroxymethyl compound) was dissolved in 250 ml EtOAc and then hydrogenated at 1 atm H_2 with 10 g 5% Pt/C as the catalyst. After 5 min about 1 eq. of H_2 was consumed. Then the catalyst was filtered off and the solvent was evaporated to yield 13.4 g of 3α-methanesulfonoxymethyl-2,4-dioxabicy-

clo[3.3.1]nonane, contaminated with the corresponding 3α-hydroxymethyl compound; ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.4 (2t, J = 4 Hz), 4.4 (m), 4.2 (d, J = 4 Hz), 3.6 (d), 3.1 (s), 1.1–2.9.

7.0 g of the product obtained was dissolved in 35 ml dry pyridine and cooled to −20°. Then 1.5 ml mesyl chloride (19.1 mmole) was added dropwise. The external cooling was removed and after 1 h 35 ml aq. 1 M $NaHCO_3$ was added. The reaction mixture was extracted with EtOAc (2 × 100 ml) and with CH_2Cl_2 (2 × 100 ml). The combined organic layers were washed with 100 ml aq 1 M $NaHCO_3$, and then dried over $MgSO_4$–K_2CO_3. After evaporation of the solvents 7.3 g pure **20** (31 mmole, 89%) was obtained; 1H NMR (60 MHz, $CDCl_3$): δ 5.4 (1 H, t, J = 4 Hz), 4.4 (2 H, m), 4.2 (2 H, d, J = 4 Hz), 3.1 (3 H, s), 1.0–2.9 (8 H).

3α-methyl-2,4-dioxabicyclo[3.3.1]*nonane* (**4**) *from 3α-methanesulfonoxymethyl-2,4-dioxabicyclo*[3.3.1]*nonane* (**20**). To a suspension of 1.7 g LAH (4.5 mmole) in 50 ml of dry diethyl ether 3.0 g of compound **20** was added in portions. After that the mixture was stirred at room temp. for 1.5 h and then under reflux for another 1.5 h. After cooling subsequently 8.5 ml EtOAc, 1.7 ml H_2O, 1.7 ml 15% NaOH and 5 ml H_2O were added dropwise. The precipitate was filtered off and washed with diethyl ether. From the combined filtrate and washings, the solvents were distilled off. The residue was distllled under vacuo to yield 760 mg pure **4** (5.4 mmole, 42%). The product obtained was identical with that obtained from the syntheses starting from cyclohexane-1,3-diol (*vide supra*).

r-1-*hydroxy*-2-*cis*-*methyl*-3-*cis*-*hydroxycyclohexane*. 2-methylcyclohexane-1,3-dione (8.0 g, 0.06 mole) was hydrogenated in 250 ml MeOH with Ra–Ni as the catalyst at 120° and 100 atm H_2. The catalyst was filtered off and the solvents were evaporated. The residue was distilled under reduced pressure to yield 5.0 g of a mixture of 2-methylcyclohexane-1,3-diol isomers; b.p. 124°/18 mm. 2.4 g of this mixture was separated by chromatography over silica (elution with $CHCl_3$–MeOH 5:1) to yield 1314.4 mg of a mixture of *r*-1-hydroxy-2-*cis*-methyl-3-*trans*-hydroxycyclohexane and *r*-1-hydroxy-2-*trans*-methyl-3-*cis*-hydroxycyclohexane and 906.1 mg of pure *r*-1-hydroxy-2-*cis*-methyl-3-*cis*-hydroxycyclohexane; ^{1}H NMR (60 MHz, $CDCl_3$): δ 3.8 (2 H, m), 3.2 (2 H, broad s), 1.0–2.1 (10 H); ^{13}C NMR (20 MHz, $CDCl_3$): δ 72.1, 38.5, 33.1, 14.6, 14.1.

9-syn-*methyl*-2,4-*dioxabicyclo*[3.3.1]*nonane* (**5**). *r*-1-hydroxy-2-*cis*-methyl-3-*cis*-hydroxycyclohexane (1.2 g, 9.2 mmole) was converted into **5** analogous to the synthesis of **3**: yield 415.8 mg (2.9 mmole, 32%); b.p. 86°/19 mm; ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.4 (1 H, d, J = −5.7 Hz), 5.0 (1 H, d, J = −5.7 Hz) 3.9 (2 H, m), 1.0–2.4 (10 H); mass spectrum (70 eV): important peaks at *m/z* 142, 141, 112, 99, 97, 95.

7α-methyl-2,4-*dioxabicyclo*[3.3.1]*nonane* (**6**). This compound was synthesized starting from 1.51 g of a mixture of *r*-1-hydroxy-3-*cis*-hydroxy-5-*cis*-methylcyclohexane and *r*-1-hydroxy-3-*trans*-hydroxy-5-*cis*-methylcyclohexane,[27] using the procedure described under the synthesis of **3**. The yield was 106.8 mg; b.p. 84–86°/20 mm; ^{1}H NMR (60 MHz, $CDCl_3$): δ 5.1 (1 H, d, J = −6.5 Hz), 4.8 (1 H, d, J = −6.5 Hz), 4.3 (2 H, m), 0.9–2.6 (10 H); mass spectrum (70 eV): important peaks at *m/z* 142, 141, 124, 99, 95, 85, 68, 41.

3α,3β-dimethyl-2,4-*dioxa*-3-*silabicyclo*[3.3.1]*nonane* (**7**). This compound was prepared as described as described in literature;[28] b.p. 35°/1.1 mm; ^{1}H NMR (100 MHz, CCl_4): δ 4.19 (2 H, m), 2.17 (2 H, m), 1.0–2.0 (6 H), 0.09 (6 H, s); mass spectrum (70 eV): important peaks at *m/z* 172, 171, 157, 129.

3α,3β-diphenyl-2,4-dioxa-3-silabicyclo[3.3.1]nonane (**8**). This compound was prepared analogous to the procedure described for compound **7**;[28] bp 104°/0.8 mm; ^{1}H NMR (100 MHz, CCl_4): δ 7.68 (4 H), 7.26 (6 H), 4.46 (2 H, m), 2.37 (2 H, m), 0.8–2.2 (6 H).

3α,3β-diphenyl-7β-t-butyl-2,4-*dioxa*-3-*silabicyclo*[3.3.1]*nonane* (**9**). Compound **9** was synthesized starting from 5-*t*-butylcyclohexane-1,3-diol[29] (mixture of epimers) using the procedure described by Pommier *et al.*;[28] b.p. 90°/1.0 mm; ^{1}H NMR (100 MHz, CCl_4): δ 7.55 (4 H), 7.25 (6 H), 4.52 (2 H, m), 1.0–2.6 (7 H), 0.76 (9 H, s), 0.07 (6 H, s).

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