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Conformational behavior of 3-borabicyclo[3.3.1]nonanes 1. Study of molecular dynamics in 3-methoxy-7α-phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]nonane

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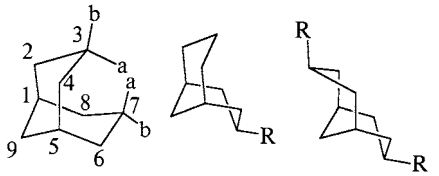
Abstract

3-Methoxy-7α-phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]nonane **5** in solution at room temperature exists in the double chair conformation, as shown by NMR studies. Increasing the temperature leads to an increase in the population of the chair–boat conformation. At decreased temperature hindered rotation around the B–O bond is observed for **5**. Dissolving **5** in deuteropyridine leads to the reversible formation of complex **6**, which exists in the chair–boat conformation. The chair–boat conformation is also the most stable one for chelate compound **7** with a tetracoordinated boron atom.

Keywords: 3-Borabicyclo[3.3.1]nonanes; Conformation; Molecular dynamics

1. Introduction

Detailed conformational analyses has been carried out for a considerable number of bicyclo[3.3.1]nonanes [1–8]. Three conformations free from bond-angle strain can be envisaged for bicyclo[3.3.1]nonanes, viz. the rigid chair–chair (*cc*), **1**, the rigid chair–boats (cb, **2** and *bc*), and the flexible double-boat (*bb*), **3** conformations [1–3]. However, the real molecules have a more complicated geometry, which is mostly controlled by strong H-3α–H-7α interactions.



1 **2** **3**

The 3β,7β-substituted compounds occur predominantly in a flattened (*cc*) conformation. A substituent in either the 3α or 7α position favors the boat conformation of the corresponding ring and this results in either a (*bc*) or (*cb*) conformation. Bulky substituents in both the 3α and 7α positions make a (*bb*) conformation the main one while, with smaller substituents, (*cb*) and (*bc*) conformations may also be populated [1–3].

Insertion of a heteroatom into a carbocycle changes the spatial characteristics for all conformations, and therefore the conformational behavior of hetero-analogues of bicyclo[3.3.1]nonanes is an interesting problem [9–12]. In particular, the introduction of a trigonal boron atom into the 3-position of the bicyclo[3.3.1]nonane skeleton substantially alters the nonbonding interactions in the molecule and therefore the character of the conformational equilibria should change compared to the carbon analogues.

Previously we have carried out a conformational analysis of a series of 3,7α-disubstituted 3-borabicy-

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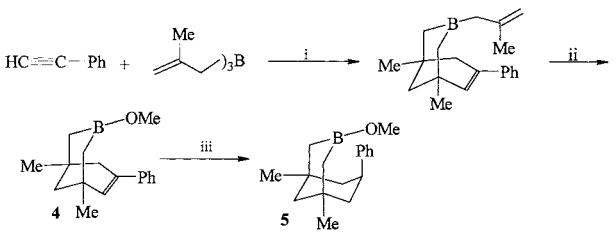
clo[3.3.1]nonanes by NMR spectroscopy [13a] and photoelectron spectroscopy [13b,c]. It was found that a flattened (*cc*) conformation is surprisingly stable for these compounds even in those cases in which the 7α-substituent is a phenyl group. This phenomenon deserves further attention because even in a cyclohexane ring the phenyl group has been found to have a strong preference for the equatorial orientation [14] (the conformational energy of a phenyl group in phenylcyclohexane was estimated to be from 11.29 [14a] to 12.29 [14b] kJ mol^{-1}). In this paper we present a detailed study of the conformational behavior of a new representative of the 3-borabicyclo[3.3.1]nonane series, viz. 3-methoxy-7α-phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]nonane **5**.

2. Results and discussion

Compound **5** was prepared by allylboron-alkyne condensation [15] of phenylethyne and *tris*(methallyl)borane followed by methanolysis and catalytic hydrogenation of the bicyclic compound **4** thus obtained (Scheme 1).



Scheme 1. Reagents and conditions: (i) 130–140°C; (ii) MeOH; (iii) H_2, $Pd/SrCO_3$.

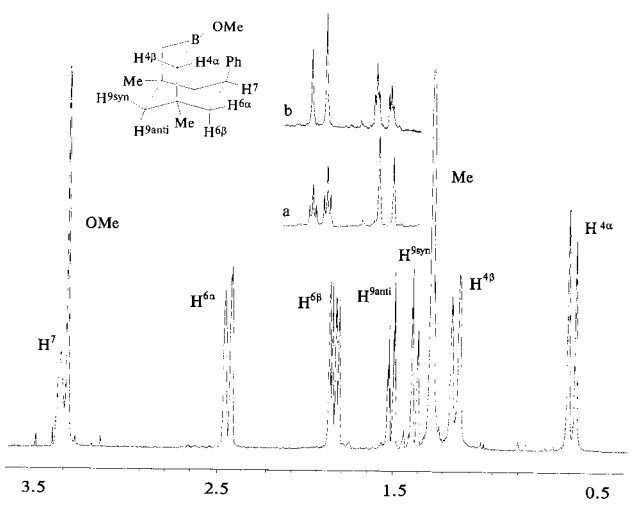


Fig. 1. ^{1}H-NMR spectrum (400 MHz, $CDCl_3$, 298 K) of compound **5**. At the top: the proton signal H-9*syn* and H-9*anti* (a) signal of (H-6α,H-8α) decoupled, (b) signal of (H-2α, H-4α) decoupled.

2.1. Analysis of the coupling constants

The coupling network in the ^{1}H-NMR spectrum of **5** (Fig. 1) was established by ^{1}H–^{1}H COSY experiments. Data on the chemical shifts and coupling constants of **5** in four different solvents are collected in Table 1.

H-7 has two vicinal couplings, viz. one with H-6α (6.0–6.3 Hz) and another with H-6β, which is 2.8–3.3 Hz. These values are characteristic for *ea* and *ee* couplings respectively [16]. They clearly indicate an equatorial orientation of H-7 and therefore the phenyl group is axial in a cyclohexane ring in a chair conformation.

The long-range *W*-coupling constants between H-6α and one of the H-9 protons, between another H-9 and one of the H-4 protons, and between H-6β and another H-4 proton allowed us to assign unambiguously the signals H-9*syn*, H-9*anti* and H-4α, H-4β because a *W*-configuration required for the existence of the long-range coupling constants can be achieved in each case in one way only. Furthermore, the analysis of the relative values of *W*-couplings ^4J(H-4α, H-6β) (2.8 Hz), ^4J(H-6α, H-9*syn*) (1.3 Hz), and ^4J(H-4β, H-9*anti*) (0.6 Hz) indicates a chair conformation for the boron ring, because for a boat conformation the largest of the three values would be expected for the latter coupling. Thus, the analysis of the coupling constants in the ^{1}H-NMR spectrum of **5** allows us to conclude that in neutral solvents at room temperature **5,** exists in a (*cc*) conformation.

2.2. Analysis of the NOESY spectrum

Independent confirmation of the predominance of a (*cc*) conformation for **5** at room temperature was obtained from the 2D NOESY experiment (see Table 2). Most informative are the NOEs between H-2β and H-9*syn*, H-4α and H-6α, and H-9*anti* and H-6β (see Fig. 2).

2.3. Study of the molecular dynamics in 5 at various temperatures

It was found that NMR spectra of **5** are temperature dependent. Fig. 3 shows a notable change in the appearance of the signal of H-6α when the temperature was raised from 293 to 343K. The chemical shift of the signal changes from 2.27 to 2.12 ppm and the value of the coupling ^3J(H-6α, H-7) increases from 3.3 to 6.0 Hz. Such a change in the coupling constant indicates the increase at high temperatures of the population of a conformation in which H-7 is axial, i.e. in the boat conformation of the carbocyclic ring of **5**

Table 1
Chemical shifts (ppm) and coupling constants (Hz) in the ^{1}H-NMR spectra of compounds **5** and **7** [a]

Proton	$CDCl_3$	C_6D_6	LT mixture [b]	C_5D_5N	**7** in $CDCl_3$
δH-4α	1.20	1.22	0.91	1.08	1.22
δH-4β	0.56	0.57	0.28	0.35	0.44
δH-6α	2.47	2.27	2.13	2.26	2.00
δH-6β	1.88	1.80	1.60	1.62	1.74
δH-7	3.38	3.18	3.10	3.12	3.00
δH-9*anti*	1.57	1.54	1.29	1.38	1.77
δH-9*syn*	1.42	1.28	1.14	1.13	1.11
δMe	1.33	1.30	1.04	1.16	1.21
δ(OMe)	3.35	3.34	3.10	3.20	-
δ(*o*-Ph)	7.70	7.49	7.41	7.55	7.41
δ(*m*-Ph)	7.56	7.39	7.27	7.42	7.56
δ(*p*-Ph)	7.41	7.28	7.13	7.28	7.73
^2J(H-4α, H-4β)	16.9	16.8	17.4	16.1	13.7
^2J(H-6α, H-6β)	14.3	13.8	13.7	14.3	13.4
^2J(H-9syn, H-9*anti*)	12.7	12.7	12.8	12.5	12.7
^3J(H-6α, H-7)	2.8	3.2	3.3	5.5	13.6
^3J(H-6β, H-7)	6.3	6.0	6.2	6.3	4.8
^4J-6α, H-9*syn*)	1.8	1.5	1.8	1.2	<0.2
^4J(H-6β, H-4β)	0.7	1.2	0.8	0.7	<0.2
^4J(H-4α, H-9*anti*)	2.7	2.8	2.9	2.6	2.4

[a] All spectra run at 303 K.
[b] CD_2Cl_2–$CDCl_3$–CCl_4 in the ratio 60:27:13. LT = low temperature.

Table 2
NOEs observed in 2D NOESY experiments on compound **5** [a]

	H-4α	H-4β	H-6α	H-6β	H-7	H-9*syn*	H-9*anti*	Me	OMe	*o*-Ph	*m*-Ph	*p*-Ph
H-4α	x	NOE	noe						noe			
H-4α	NOE	x				noe		noe	noe			
H-6α	noe		x	NOE	NOE			noe		noe		
H-6β			NOE	x	NOE		noe	noe				
H-7			NOE	NOE	x							
H-9*syn*		noe				x	NOE	noe				
H-9*anti*				noe		NOE	x	noe				
Me		noe	noe	noe		noe	noe	x				
OMe	noe	noe							x			
o-Ph			noe							x		
m-Ph											x	
p-Ph												x

[a] NOEs written in capitals are obvious cross-peaks, i.e. between the signals which have cross-peaks in the COSY spectrum.

(see Scheme 2). This effect is probably caused by the increased steric requirements of the phenyl group at higher temperatures.

Fig. 4 demonstrates spectral dynamics in the ^{13}C-NMR spectra of **5**. One can see that four signals, viz. of C-2, C-6, C-1, and CH_3, observed at room temperature as single peaks, are split at low temperatures into two signals with equal intensity.

This effect is induced by hindered rotation about the B–O bond due to the overlap of the sp^3-hybridized lone

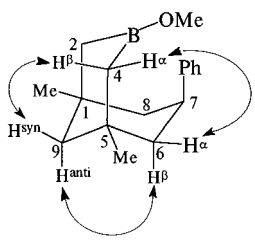


Fig. 2. NOEs indicative of the (*cc*) conformation of **5** in $CDCl_3$ at 298 K.

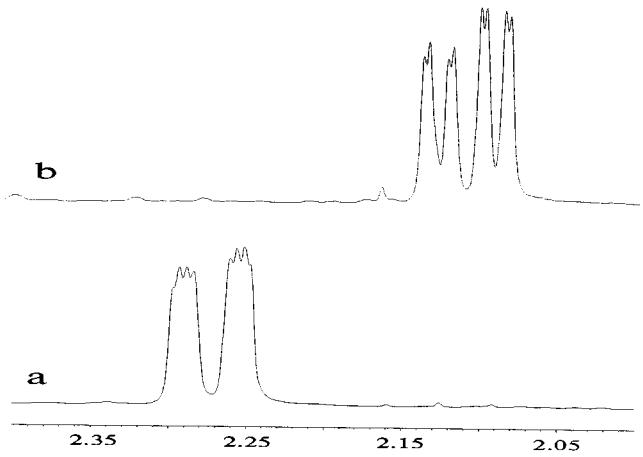
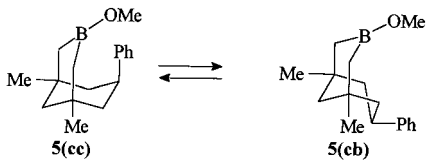


Fig. 3. Signal of the proton H-6α, H-8α in the ^{1}H-NMR spectrum (C_6D_6, 400 MHz). (a) Of **5** at 293°K; (b) at 343°K.



Scheme 2.

pair on oxygen with the vacant p-orbital of boron. Similar effects were earlier observed for $MeOBMe_2$ and $(Me_2B)_2O$ [16]. An account of a quantitative study of the activation barriers for hindered rotation around the B–O bond in different 3-borabicylo[3.3.1]nonanes will be presented in a separate paper.

2.4. The influence of complexation on the conformational equilibrium

In Table 3 the temperature dependence of the ^{11}B chemical shift of a solution of **5** in deuteropyridine is shown. The chemical shift of boron changes from 19.4 ppm at 246 K to 53.1 ppm at 348 K. The latter value is similar to that for parent compound **5,** the chemical shift of which in $CDCl_3$ is 53.4 ppm and is almost independent of the temperature. The change in ^{11}B chemical shift with decreasing temperature reflects the shift of the equilibrium between **5** and **6** in favor of the latter.

Fig. 5 displays the appearance of the signal of H-6α in the ^{1}H-NMR spectrum of **5** in deuteropyridine at different temperatures. According to the previous discussion, the changes in the spectrum taking place when the temperature is decreased reflect the shift of the equilibrium (Scheme 3) in favor of the pyridine complex **6**. The most dramatic change is observed for the coupling ^3J(H-6α, H-7), from approximately 12 Hz at 246 K (Fig. 4(a)) to 5.5 Hz at room temperature (Fig. 4(d)). The former value is characteristic for *aa* couplings in cyclohexane rings [17], which means that at 246 K the boat conformation of the carbocyclic ring of **6** is the most stable one.

In the low-temperature ^{13}C-NMR spectrum of **5** in deuteropyridine, no splittings of signals similar to those observed for solution of **5** in a neutral solvent were observed. This is not surprising because in **6** the p-orbital of boron is already occupied by the lone pair of pyridine, and overlap with the lone pair on oxygen does not occur.

Thus, it can be concluded that it is the formation of complex **6** that leads to a change in the conformational preferences of compound **5**, making the boat conformation of the carbocyclic ring the most stable one. This is caused by the transformation of the trigonal sp^2-hybridized boron atom in **5** to the tetragonal sp^3-hybridized boron atom in **6**. The spatial characteristics of an sp^3-hybridized boron atom should be substantially the same as those for a carbon atom, so the stability of the (*cb*) conformation found for **6** is in a good accord with the conformational properties of 3α,7α-disubstituted bicyclo[3.3.1]nonanes.

The latter statement is further supported by the conformational analysis of a stable compound with a tetracoordinated boron atom, viz. dibenzoylmethanochelate **7**, which we prepared from **5** (Scheme 4).

The chemical shifts and coupling constants observed in the ^{1}H-NMR spectrum of **7** are given in Table 1. The coupling ^3J(H-6α, H-7) is 13.4 Hz, which indicates the axial location of H-7, and therefore the equatorial orientation of the phenyl group. Thus the carbocyclic ring of **7** is in a boat conformation. This conclusion is strongly supported by the results of 2D NOESY exper-iments (see Table 4, Fig. 6), in which a long-range (five bonds) NOE between H-7 and H-9*anti* was observed. The chair conformation of the boracyclic ring follows, from arguments similar to those in the previous discussion, from the *W*-coupling ^4J(H-4α, H-9*anti*) = 2.4 Hz and the NOE between H-4β and H-9*syn* (see Fig. 6).

3. Conclusions

The conformational analysis of 3-methoxy-7-phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]nonane **5** shows that at room temperature the (*cc*) conformation is the most stable one for this compound. An increase in temperature leads to a shift of the conformational equilibrium, which increases the population of the (*cb*) conforma-

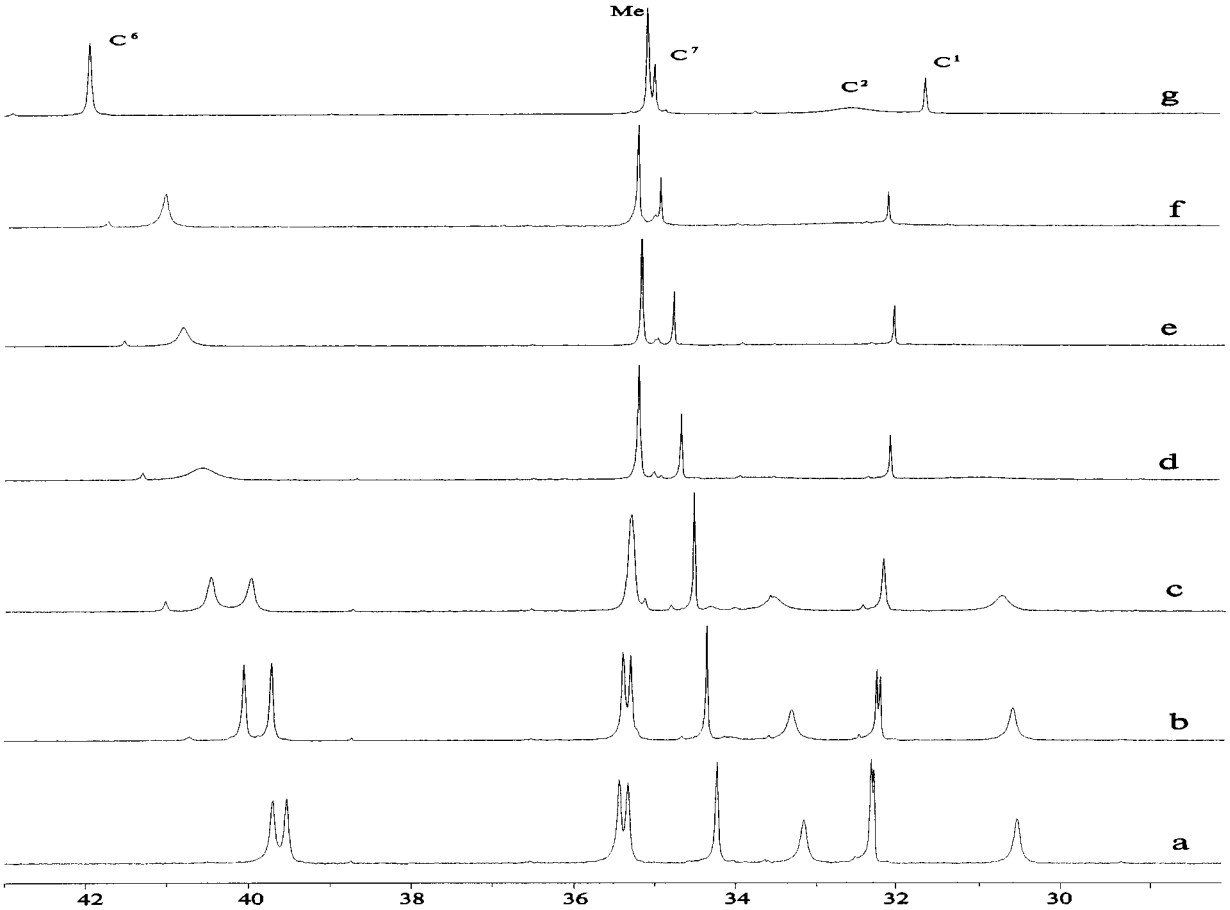


Fig. 4. Section plots of ^{13}C-NMR spectra (low-temperature mixture of solvents, 100 MHz) of **5** at different temperatures. (a) $T = 193$°K; (b) $T = 218$°K; (c) T = 230°K; (d) $T = 239$°K; (e) $T = 261$°K; (f) $T = 273$°K; (g) $T = 298$°K.

tion. The transformation of the boron atom into a tetracoordinated state, either by complexation with pyridine or by formation of a chelate compound **7,** leads to a change in conformational preferences, making the (*cb*) conformation the most stable one.

4. Experimental

4.1. 3-Methoxy-7α-phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]non-6-ene ***4***

Phenylethyne (5.2 g, 0.051 mol) was added dropwise to *tris*(methallyl)borane (9.05 g, 0.05l mol) at 145–155°C. The mixture was heated for 15 min, then cooled to ambient temperature and methanol (5 ml) was added. The mixture was heated under reflux for 20 min, the excess of methanol was removed in vacuo and the residue was distilled to give **4** (9.9 g, 73%), b.p. 122–123°C (1 torr). Found, C, 80.67; H, 9.42; B, 4.28%. Calculated, for $C_{17}H_{23}BO$ is, C, 80.33; H, 9.12; B, 4.25%.

Table 3
Chemical shifts ^{11}B (δ, ppm) of **5** in deuteropyridine

T (K)	δ^{11}B
246	19.4
255	27.6
270	37.4
303	49.0
338	52.9
348	53.1

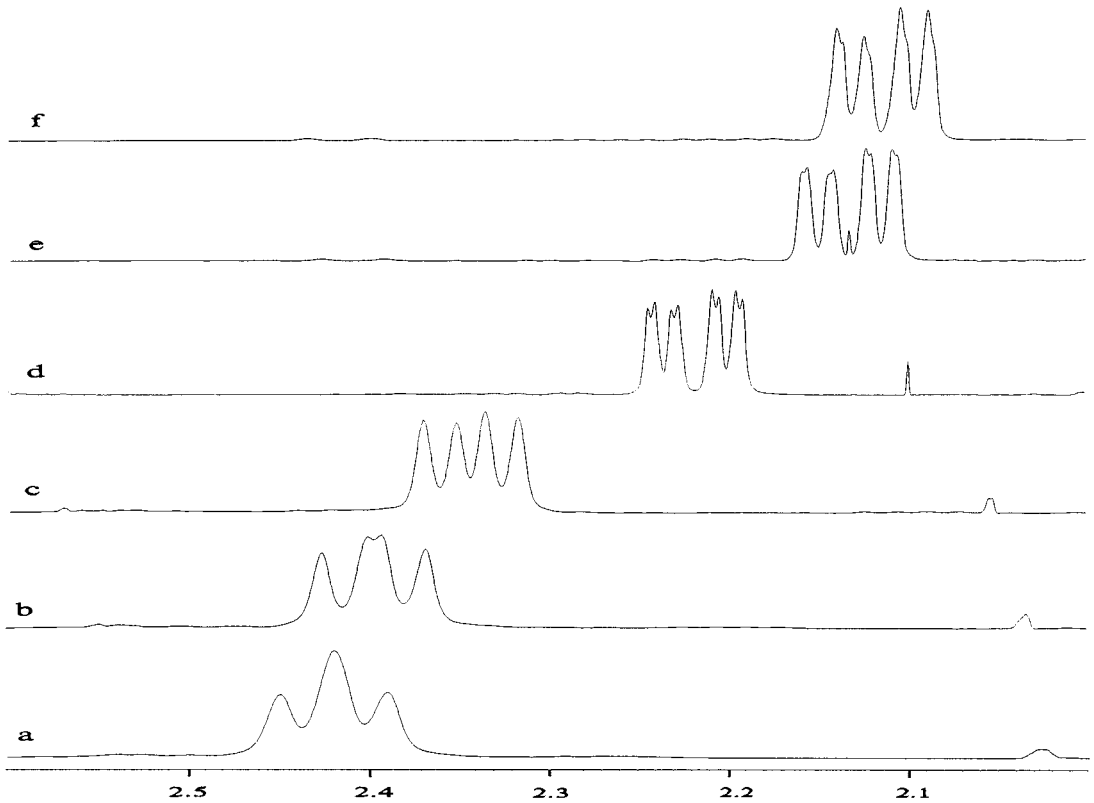
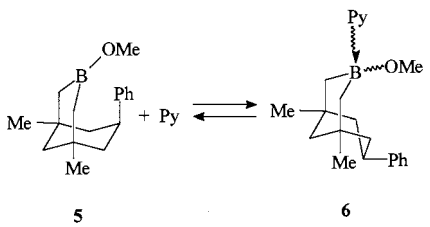
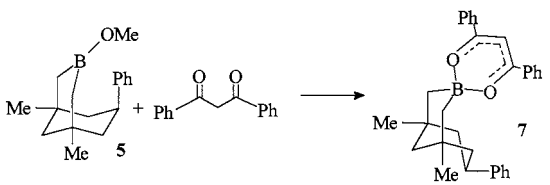


Fig. 5. Temperature dependence of the signal of H-6α, H-8α proton in the ^{1}H-NMR spectrum of **5** (C_5D_5N, 400 MHz): (a) $T = 246$ K; (b) $T = 255$ K; (c) $T = 270$ K; (d) $T = 303$ K; (e) $T = 338$ K; (f) $T = 348$ K.



Scheme 3.



Scheme 4.

4.2. 3-Methoxy-7-phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]nonane **5**

A solution of **1** (9 g, 0.035 mol) in absolute methanol (10 ml) was hydrogenated over 5% Pd on $SrCO_3$ (0.50 g). A total of 900 ml of hydrogen were absorbed. After filtration, the solvent was removed and the residue was distilled in vacuo to give **5**, (8.44 g, 93%) b.p. 121–122°C (1 torr), n_D^{20} 1.5322. Found, C, 79.54; H, 9.89; B, 4.34%. Calculated for $C_{17}H_{25}BO$ is C, 79.70; H, 9.84; B, 4.22%.

4.3. 7-Phenyl-1,5-dimethyl-3-borabicyclo[3.3.1]nonyl benzoylacetophenoate 7

To a solution of dibenzoylmethane (0.95 g, 0.0047 mol) in ether (10 ml) was added **5** (1.21 g, 0.0047 mol). After 1 h orange crystals precipitated. Ether was distilled off and the precipitate was washed with hexane to give **7**, (1.9 g, 100%) m.p. 198–200°C. Found, C, 83.05; H, 7.40; B, 2.65%. Calculated for $C_{31}H_{33}BO_3$, is C, 83.04; H, 7.42; B, 2.41%.

Acknowledgements

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Table 4
NOEs observed in 2D NOESY experiments for compound **7** [a]

	H-4α	H-4β	H-6α	H-6β	H-7	H-9*syn*	H-9*anti*	Me	*o*-Ph	*m*-Ph	*p*-Ph
H-4α	x	NOE	noe								
H-4β	NOE	x									
H-6α	noe		x	NOE					noe		
H-6β			NOE	x	NOE			noe			
H-7				NOE	x		noe		noe		
H-9*syn*		noe				x	NOE				
H-9*anti*					noe	NOE	x				
Me		noe		noe				x			
o-Ph			noe		noe				x		
m-Ph										x	
p-Ph											x

[a] NOEs written in capitals are obvious cross-peaks, i.e. between the signals which have cross-peaks in the COSY spectrum.

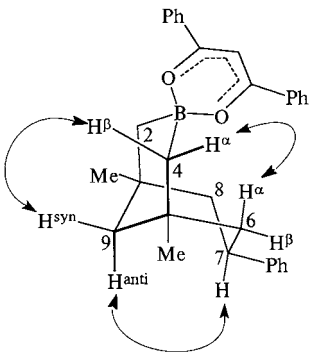

Fig. 6. Elucidation of the stable (*cb*) conformation of **7** from long-range couplings and NOE data.

References

[1] J.A. Peters, J.M. Van der Toorn, H. Van Bekkum, Tetrahedron 31 (1975) 2273.
[2] J.A. Peters, J.M. Van der Toorn, H. Van Bekkum, Tetrahedron 33 (1977) 349.
[3] J.A. Peters, J.M.A. Baas, B. Van der Graaf, J.M. Van der Toorn, H. Van Bekkum, Tetrahedron 34 (1978) 3313.
[4] H.J. Schneider, W. Ansorge, Tetrahedron 33 (1977) 265.
[5] Y. Senda, J.I. Ishiyama, S. Imaizumi, J. Chem. Soc. Perkin Trans. 2 (1981) 90.
[6] A. Henmann, H. Kolshorn, Tetrahedron 31 (1975) 1571.
[7] H. van Oosterhont, C. Kruk, W.N. Speckamp Tetrahedron Lett. 19 (1978) 653.
[8] H.J. Schneider, M. Lonsdorfer, E.F. Weigand, Org. Magn. Res. 8 (1976) 363.
[9] J.A. Peters, P.E.J. Peters-Van Granenburgh, J.M. Van der Toorn, Th.M. Wortel, H. Van Bekkum, Tetrahedron 34 (1978) 2217.
[10] Th.R. Bok, W.N. Speckamp, Tetrahedron 35 (1979) 267.
[11] P.C. Ruenitz, J. Org. Chem. 43 (1978) 2910.
[12] P.J. Cox, P.H. McCabe, N.J. Milne, G.A. Sim, J. Chem. Soc. Chem.Commun. (1985) 626.
[13] (a) M.E. Gursky, A.S. Shashkov, B.M. Mikhailov, J. Organomet. Chem. 199 (1980) 171. (b) R.E. Wiesmann, P. Rademacher, Chem. Ber. 127 (1994) 509. (c) R.E. Wiesmann, P. Rademacher, Chem. Ber. 127 (1994) 1105.
[14] (a) M.E. Squillacote, J.M. Neth, J. Am. Chem. Soc. 109 (1987) 198. (b) E.L. Eliel, M. Monoharan, J. Org. Chem. 46 (1981) 1959.
[15] B.M. Mikhailov, Yu.N. Bubnov, Organoboron Compounds in Organic Synthesis, Harwood Academy Science Publishing, Chur, 1984.
[16] H. Gunter, NMR-Spectroscopie, Georg Thieme Verlag, Stuttgart, 1973.
[17] G.F. Lanthier, W.A.G. Graham, J. Chem. Soc. Chem. Commun. (1968) 715.