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Stereochemistry of Seven-Membered Heterocycles: XLVI.* Synthesis and Dynamic ^{13}C NMR Spectroscopy of Spiro[cyclohexane-1,4′-[3,5]dioxabicyclo[5.1.0]octanes]. DFT Calculations of Structurally Related Formaldehyde and Acetone Acetals

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Abstract—Spiro[cyclohexane-1,4′-[3,5]dioxabicyclo[5.1.0]octanes] were synthesized, and their conformational behavior was studied by dynamic ^{13}C NMR spectroscopy. Anancomeric displacement of conformational equilibrium toward two nonequivalent *twist* conformers with close energies was revealed. The relative Gibbs energies ΔG^{o} and enthalpies of formation ΔH^{o} of *twist* and *chair*-like conformers with *endo* and *exo* orientation of the three-membered ring of structurally related formaldehyde and acetone acetals were calculated in terms of the density functional theory at the B3LYP/6-31G(*d*,*p*) level. Like spiro-cyclohexane analogs, they were shown to have a non-*chair* conformation.

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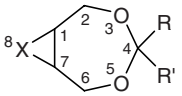
Up to know, data have been reported on the synthesis and steric structure of various bicyclic compounds in which a seven-membered cyclic acetal fragment is fused to a three-membered carbo- or heterocycle {X = O [2–5], NR [6, 7], CH_2 [2, 3, 8, 9], CCl_2 [8, 10–13], CBr_2 [13–15], $C(CO_2R)_2$ [16], $CHCO_2R$ [17–19]}. Insofar as the three-membered ring may be regarded as a specific substituent [5, 13], the existence of stereoisomers is possible when $R \neq R'$.



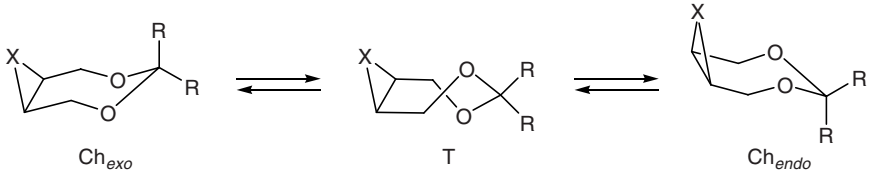
For such systems, the set of conformers is confined to two *chair*-like structures of the seven-membered ring with *exo* and *endo* orientations of the three-membered ring (Ch_{exo} and Ch_{endo}) and *twist* structure (T) (Scheme 1).

In continuation of our studies on stereochemical relations holding in the series of 3,5-dioxabicyclo[5.1.0]octane derivatives [5, 9, 13, 15, 19], in the present work we examined the conformational behavior of spirocyclic acetals **I–V** by dynamic ^{13}C NMR spectroscopy. Functionally substituted cyclopropanes are widely used in synthetic practice [20], while ketals **III** and **V** must be considered as latent 1,2-bis(hydroxymethyl)cyclopropanes, for cyclohexanone is known to be used to protect glycols [21].

Before proceeding with experimental studies, we calculated the relative enthalpies of formation ΔH^{o} and Gibbs energies ΔG^{o} of conformers Ch_{exo}, Ch_{endo}, and T. As models we selected formaldehyde acetals **VI–X** and acetonides **XI–XV**. Steric effect of hydrogen atoms at the acetal carbon atom on conformational behavior of compounds **VI–X** is minimal. By contrast, the presence of two geminal methyl groups in molecules **XI–XV** should largely determine the relative stabilities of different conformers; in particular, *chair*-like conformers should be destabilized as a result of 1,3-*syn*–axial $CH_3 \cdots H$ repulsion. The calculated values of ΔG^{o} and ΔH^{o} of different conformers of compounds **VI–XV** are given in table. The calculations were performed in terms of the density functional theory (DFT)

* For communication XLV, see [1].

Scheme 1.



I–XV

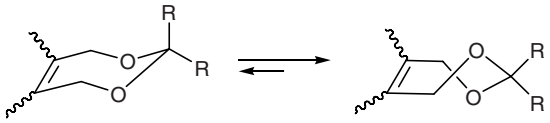
I–V, RR = $(CH_2)_5$; **VI–X**, R = H; **XI–XV**, R = Me; **I**, **VI**, **XI**, X = O; **II**, **VII**, **XII**, X = S; **III**, **VIII**, **XIII**, X = CCl_2; **IV**, **IX**, **XIV**, X = CHCl; **V**, **X**, **XV**, X = CH_2.

using B3LYP/6-31G(*d*,*p*) basis set (Gaussian 98 software package [22]) with full geometry optimization without symmetry restrictions. Second derivative matrices were calculated for all stationary point. All structures under discussion are characterized by only positive vibration frequencies. No scaling factors [23] were introduced.

The data obtained for formaldehyde acetals **VI–X** show that any conformer among Ch$_{exo}$, Ch$_{endo}$, and T may be the most favorable, depending on the X fragment. Only when X = CCl_2 or CHCl (the C–Cl bond is oriented *endo*), the relative stabilities of conformers are generally predictable and are controlled by obvious steric repulsions involving the C–Cl and C–O bonds. The experimental (IR, ^{1}H and ^{13}C NMR, and X-ray diffraction) data for oxirane **VI** [4, 5], thiirane **VII** [24], and cyclopropanes **VIII** [13] and **X** [9] are very consistent with the results of calculations.

Conformational equilibria between the *chair* and *twist* forms of seven-membered acetonides (R = Me) with a planar carbocyclic fragment (such as 2,2-dimethyl-1,3-dioxacyclohept-5-ene, its benzo-fused derivative [25–27], and their analogs) were shown to be displaced toward the latter. Cyclic acetals derived from cyclohexanone [RR = $(CH_2)_5$] are conformational analogs of acetonides [26, 28, 29], and the seven-membered ring therein adopts exclusively *twist* conformation (Scheme 2). Therefore, it seemed to be quite reasonable to perform a comprehensive conformational analysis of 4,4-dialkyl-substituted 3,5-dioxabicyclo[5.1.0]octanes **I–V** and **XI–XV**, including theoretical study of relatively simpler acetonides **XI–XV** and experimental study by ^{13}C NMR spectroscopy on the behavior of spiro acetals **I–V**. The presence of a pentamethylene fragment in the latter was expected to provide more detailed information on their steric structure.

Scheme 2.



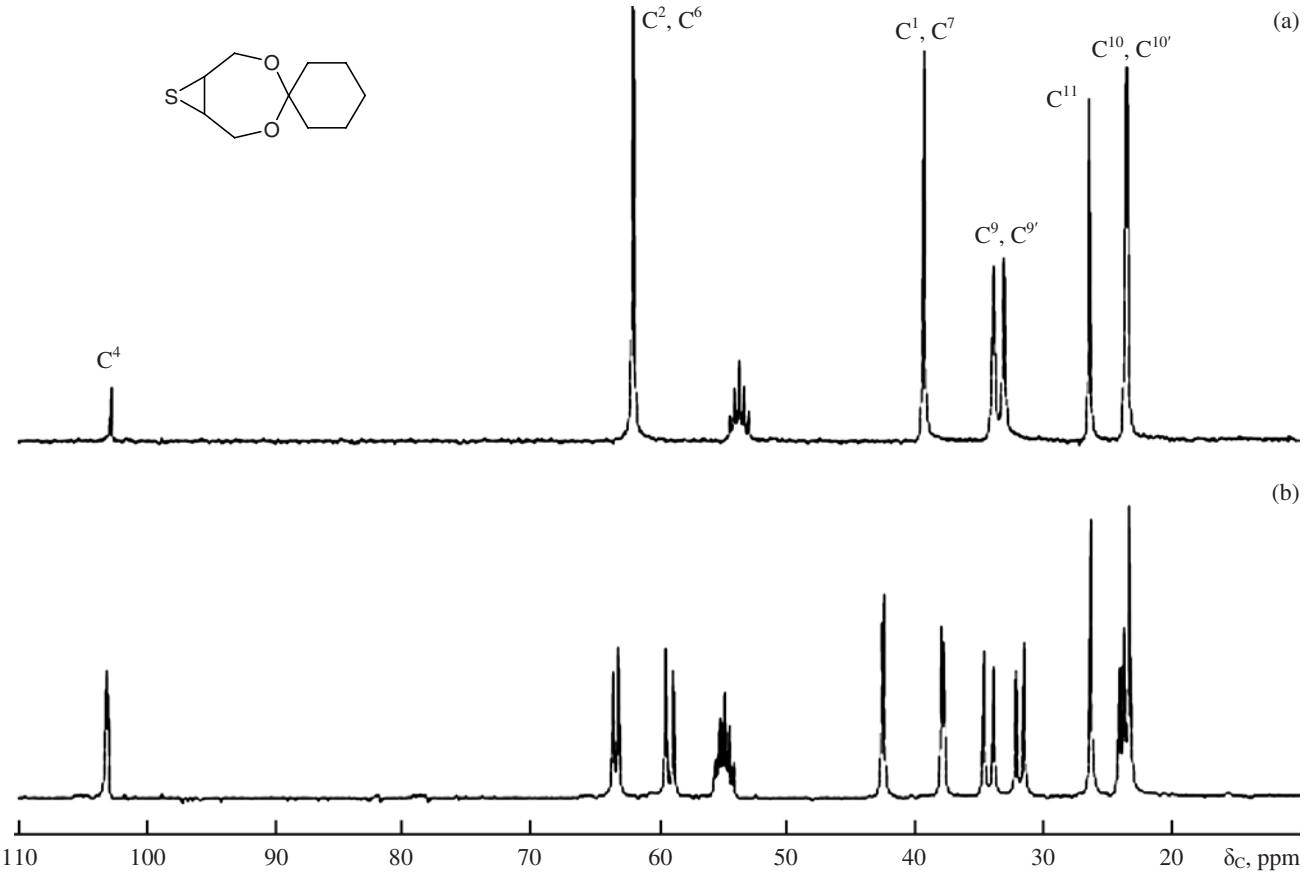
It was found that all acetonides **XI–XV** prefer a non-*chair* conformation, in keeping with published data for their planar analogs (see above). Replacement of hydrogen atoms on the acetal carbon atom by methyl groups, other conditions being equal does not affect the conformational equilibrium Ch$_{exo}$ ⇄ Ch$_{endo}$ (see table). This is very important from the viewpoint of estimating reliability of the theoretical data.

As follows from the dynamic ^{13}C NMR spectra, acetals **I–IV** at low temperature give rise to equilibria

Relative Gibbs energies ΔG^o and enthalpies of formation ΔH^o (in parentheses), kcal/mol, of Ch$_{exo}$, Ch$_{endo}$, and T conformers of bicyclo[5.1.0]octanes **VI–XV**, calculated by the B3LYP/6-31G(*d*,*p*)//B3LYP/6-31G(*d*,*p*) method

Conformer	**VI**	**VII**	**VIII**	**IXa**[a]	**IXb**[b]	**X**	**XI**	**XII**	**XIII**	**XIVa**[a]	**XIVb**[b]	**XV**
Ch$_{endo}$	0.50 (0.57)	1.02 (1.15)	3.37 (3.91)	3.36 (3.65)	0 (0)	0 (0)	3.18 (2.80)	2.30 (2.07)	4.48 (4.23)	4.40 (4.38)	0.94 (0.65)	0.84 (0.55)
Ch$_{exo}$	1.10 (0.89)	0 (0)	0 (0)	0 (0)	2.61 (2.54)	1.77 (1.58)	3.65 (3.24)	0,59 (0.28)	1,63 (1.40)	0.86 (0.66)	3.33 (3.06)	2.21 (1.82)
T	0 (0).00	1.49 (1.71)	0.86 (1.14)	1.65 (1.90)	1.67 (1.79)	5.40 (5.83)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

[a] *endo* Orientation of the C–Cl bond.
[b] *exo* Orientation of the C–Cl bond.



^{13}C NMR spectra of spiro[cyclohexane-1,4′-[3,5]dioxa[8]thiabicyclo[5.1.0]octane] (**II**) in CS_2–CD_2Cl_2 (2:1) at (a) 25°C and (b) –110°C.

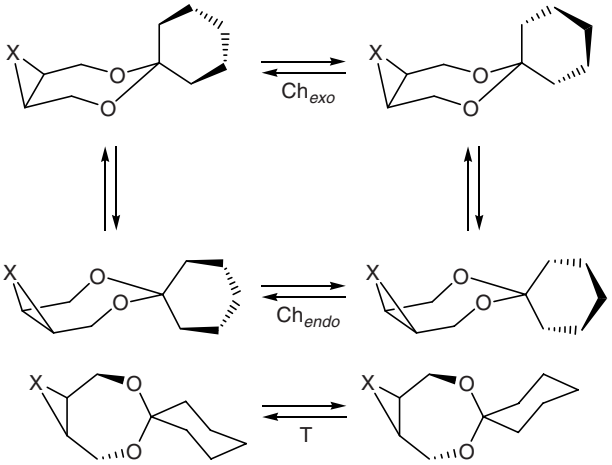
between two conformers at ratios of 56:44 (**I**), 56:44 (**II**), 52:48 (**III**), and 64:36 (**IV**). The ΔG^o values range from 0.1 to 0.2 kcal/mol, i.e., the conformers have fairly similar energies. No exchange-induced signal broadening was observed in the spectra of **V** in the temperature range from −25 to −85°C. Illustrative are the ^{13}C NMR spectra of thiirane **II** shown in figure. At room temperature, the C^1/C^7, C^2/C^6, and C^4 atoms give rise to singlets which are converted into more complex signals at –110°C: the spiro carbon signal becomes a doublet, and those from C^1/C^7 and C^2/C^6 look like two pairs of lines with different intensities. Analogous spectral pattern is typical of $C^9/C^{9'}$ and $C^{10}/C^{10'}$ with the difference that the C^{10} and $C^{10'}$ carbon atoms are nonequivalent even at room temperature. Only the signal from the C^{11} atom which is most distant from the heterocyclic moiety shifts insignificantly.

Only one diastereoisomeric monochloro derivative **IV** was studied experimentally. Its steric configuration is readily determined on the basis of the ^{1}H NMR data. The 8-H signal (δ 3.34 ppm) appears as a well resolved triplet with a coupling constant $^3J_{HH}$ of 7.4 Hz typical of *endo* isomers [30, 31]; *exo* isomers are characterized by considerably smaller spin–spin coupling constants ($^3J_{HH} \approx 3$–4 Hz).

The observed low-temperature ^{13}C NMR spectra (slow exchange) reflect two kinds of conformational equilibria. In the first of these, stereoisomerism involves *chair* conformers of both seven- and six-membered rings (the latter is assumed to have *chair* conformation *a priori*). Here, *endo* and *exo* orientations of the three-membered ring each give rise to two isoenergetic enantiomeric structures. In the second case, the seven-membered acetal ring adopts a *twist* conformation, and conformations of the cyclohexane ring are radically different.

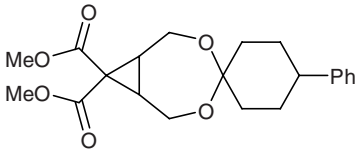
It is hardly probable to prefer *chair*-like or flexible conformers of seven-membered acetals on the basis of the obtained spectral parameters which are very similar. On the other hand, convincing proofs in favor of equilibria involving just non-*chair* structures may be derived from the calculation data (see table). Taking

Scheme 3.

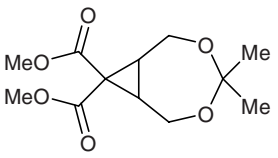


into account the calculated parameters of acetonides **I–IV**, considerable prevalence of one of the Ch_{exo} and Ch_{endo} conformers should be expected provided that the equilibrium $Ch_{exo} \rightleftarrows Ch_{endo}$ exists. The distant three-membered ring in the *twist* conformer cannot induce appreciable energy differentiation of the conformers resulting from inversion of the six-membered carbocycle (Scheme 3); this is confirmed by fairly similar ΔG values for equilibrium structures observed in the low-temperature spectra. The same equally applies to acetal **V**, and it is reasonable to assume that acetal **V** also has non-*chair* structure.

There is only one publication on the structure of related spirocyclic acetal **XVI** [16]. According to the calculations performed with the use of Desktop Molecular Modeller on PC-Windows platform and ^{1}H NMR spectra at room temperature, the Ch_{exo} conformer was found to be the most stable. This result contradicts our data. Following the above approach we analyzed the behavior of the corresponding acetonide **XVII**. As might be expected, the *chair*-like conformers turned out to be unfavorable in both equilibria, $Ch_{exo} \rightleftarrows T$ and $Ch_{endo} \rightleftarrows T$ ($\Delta\Delta G°$ = 3.35 and 5.82 kcal/mol, respectively).



XVI



XVII

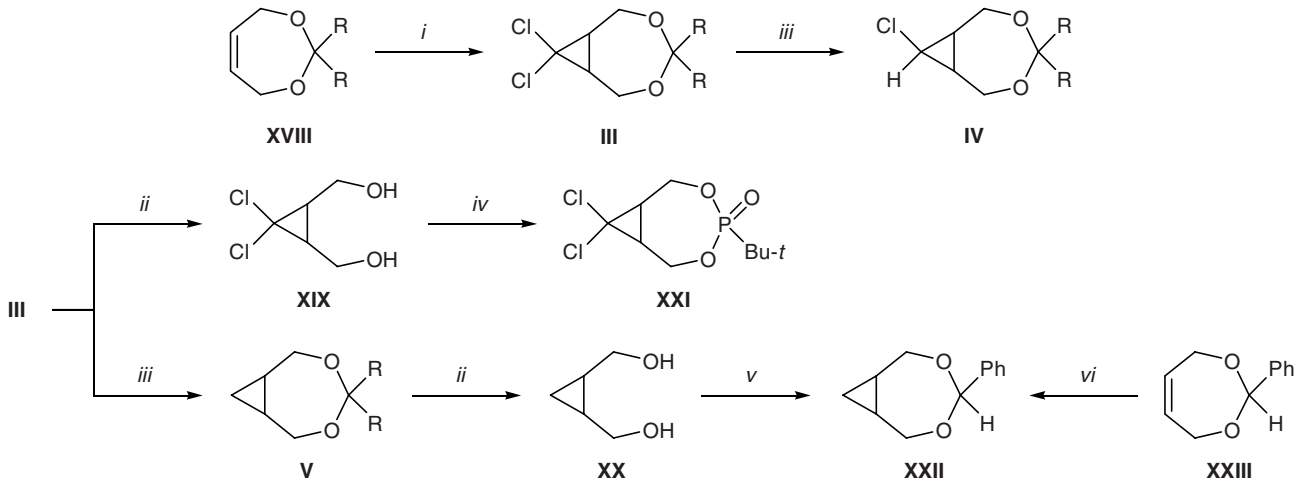
Let us consider the synthesis of compounds **I–V** (Scheme 4). Thiirane derivative **II** was prepared by sulfurization of oxirane **I** with thiourea according to the procedure described in [24]. Acetal **III** was prepared by dichlorocyclopropanation of the corresponding spirocyclic olefin **XVIII** according to Makosza and was then hydrogenated with lithium in *tert*-butyl alcohol [9, 32]. Compound **V** was isolated by column chromatography; in addition, minor (~10%) *endo*-chloro derivative **IV** was isolated. Hydrolysis of acetals **III** and **V** in aqueous tetrahydrofuran gave the corresponding *cis*-1,4-diols **XIX** and **XX**. Compound **XX** was synthesized previously according to Simmons–Smith through silylated but-2-ene-1,4-diol [33] or by reduction of *cis*-cyclopropane-1,2-dicarboxylic acid or its esters [34–36]. A specific stereochemical technique was used in [36] where *cis*-diol **XX** was isolated from a mixture of diastereoisomeric 1,2-bis(hydroxymethyl)-cyclopropanes via condensation with cyclohexanone, followed by hydrolysis. We synthesized diol **XX** from accessible 1,3-dioxacycloheptene **XVIII** through acetals **III** and **V**; this procedure also seems to be quite acceptable for laboratory practice. 1,2-Bis(hydroxymethyl)cyclopropanes **XIX** and **XX** were used as starting materials for the synthesis of seven-membered phosphonate **XXI** and benzaldehyde acetal **XXII**.

Thus, using DFT calculations and dynamic ^{13}C NMR spectroscopy, 4,4-dimethyl(pentamethylene)-3,5-dioxabicyclo[5.1.0]octanes having carbon, oxygen, and sulfur atoms were shown to exist in *chair–twist* equilibrium displaced toward anancomeric non-*chair* conformer. Analogous pattern was observed previously for seven-membered acetals having a planar fragment as a result of unfavorable 1,3-*syn*-axial interactions in alternative *chair*-like conformers.

EXPERIMENTAL

The ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on a Varian Unity-300 spectrometer at 300, 75.43, and 121.42 MHz, respectively. The chemical shifts were measured relative to HMDS (^{1}H, ^{13}C) or 85% H_3PO_4 (external, ^{31}P). The low-temperature ^{13}C NMR spectra were obtained with the aid of a B-VT-1000 temperature-controlling unit (pulse width 20–30°, broad-band decoupling from protons, digital exponential filtration, *lb* = 2–4 Hz; pulse delay *dl* = 1–2 s, *sw* = 200 ppm, *nt* 400 to 1000). The mass spectrum (electron impact, 70 eV) was recorded on a Finnigan MAT-212 mass

Scheme 4.



RR = $(CH_2)_5$; *i*: $CHCl_3$–50% aq. NaOH–$Et_3BzlNCl$; *ii*: 0.1 N hydrochloric acid–THF; *iii*: Li–*t*-BuOH; *iv*: *t*-$BuPCl_2$–O_2; *v*: PhCHO–$[H^+]$; *vi*: CH_2I_2–Zn/Ag.

spectrometer with direct sample admission into the ion source.

Spiro[cyclohexane-1,4′-[3,5,8]trioxabicyclo-[5.1.0]octane] (I) was synthesized according to [12]. bp 147–149°C (20 mm); published data [37]: bp 133°C (15 mm). ^{13}C NMR spectrum (CS_2–CD_2Cl_2, 2:1), δ_C, ppm: at 25°C: 56.61 (C^1, C^7), 59.42 (C^2, C^6), 102.24 (C^4), 32.51 and 33.95 (C^9, $C^{9'}$), 23.29 and 23.42 (C^{10}, $C^{10'}$), 26.23 (C^{11}); at −90°C: major conformer: 57.56 (C^1, C^7), 58.20 and 60.28 (C^2, C^6), 102.39 (C^4), 31.19 and 34.68 (C^9, $C^{9'}$), 23.24 and 23.57 (C^{10}, $C^{10'}$), 26.21 (C^{11}); minor conformer: 56.35 (C^1, C^7), 57.56 and 60.67 (C^2, C^6), 32.22 and 33.62 (C^9, $C^{9'}$), 23.18 and 23.82 (C^{10}, $C^{10'}$).

Spiro[cyclohexane-1,4′-[3,5]dioxa[8]thiabicyclo-[5.1.0]octane] (II). A solution of 4.54 g (24.6 mmol) of compound **I** and 3.61 g (47.4 mmol) of thiourea in 50 ml of methanol was heated for 48 h under reflux. The mixture was then kept for 12 h at room temperature, the precipitate was filtered off and washed with warm petroleum ether on a filter, the filtrate was concentrated, and the precipitate was filtered off and recrystallized from petroleum ether. Yield 3.09 g (63%), mp 50–52°C. ^{13}C NMR spectrum (CS_2–CD_2Cl_2, 2:1), δ_C, ppm: at 25°C: 39.30 (C^1, C^7), 61.98 (C^2, C^6), 102.77 (C^4), 33.04 and 33.85 (C^9, $C^{9'}$), 23.38 and 23.52 (C^{10}, $C^{10'}$), 26.36 (C^{11}); at −110°C: major conformer: 37.91 and 42.41 (C^1, C^7), 59.43 and 63.12 (C^2, C^6), 103.14 (C^4), 31.47 and 34.61 (C^9, $C^{9'}$), 23.23 and 23.67 (C^{10}, $C^{10'}$), 26.25 (C^{11}); minor conformer: 37.70 and 42.54 (C^1, C^7), 58.83 and 63.54 (C^2, C^6), 102.98 (C^4), 32.07 and 33.85 (C^9, $C^{9'}$), 24.02 (C^{10}, $C^{10'}$). Found, %: C 59.92; H 8.58; S 16.13. $C_{10}H_{16}O_2S$. Calculated, %: C 59.97; H 8.05; S 16.01.

8′,8′-Dichlorospiro[cyclohexane-1,4′-[3,5]dioxabicyclo[5.1.0]octane] (III). A solution of 30 g (0.178 mol) of acetal **XVIII** [37] and 1.22 g of benzyl (triethyl)ammonium chloride in 113 ml of chloroform was cooled to 0°C, and 57.4 g of 50% aqueous sodium hydroxide was added dropwise over a period of 1 h under vigorous stirring. The mixture was vigorously stirred for 7 days and filtered, and the organic phase was separated, dried over magnesium sulfate, and concentrated. The residue was distilled under reduced pressure. Yield 36.5 g (81%), thick oil, bp 170–175°C (20 mm). ^{13}C NMR spectrum (CS_2–CD_2Cl_2, 2:1), δ_C, ppm: at 25°C: 34.74 (C^1, C^7), 57.69 (C^2, C^6), 103.45 (C^4), 64.20 (C^8), 33.10 and 34.56 (C^9, $C^{9'}$), 23.24 and 23.34 (C^{10}, $C^{10'}$), 26.21 (C^{11}); at −100°C: major conformer: 34.15 and 34.47 (C^1, C^7), 57.32 and 57.58 (C^2, C^6), 103.61 (C^4), 64.54 (C^8), 31.07 and 33.46 (C^9, $C^{9'}$), 22.95 and 23.61 (C^{10}, $C^{10'}$), 26.19 (C^{11}); minor conformer: 33.87 and 35.84 (C^1, C^7), 56.94 and 58.21 (C^2, C^6), 33.25 (C^9, $C^{9'}$), 23.13 (C^{10}, $C^{10'}$). Found: $[M]^+$ 250.052. $C_{11}H_{16}Cl_2O_2$. Calculated: *M* 250.052.

8′-Chlorospiro[cyclohexane-1,4′-[3,5]dioxabicyclo[5.1.0]octane] (IV) and spiro[cyclohexane-1,4′-[3,5]dioxabicyclo[5.1.0]octane] (V). Finely cut metallic lithium, 0.8 g (110 mmol), was added in portions under stirring to a solution of 2.43 g (9.7 mmol) of compound **III** and 8 g (110 mmol) of *tert*-butyl alcohol in 40 ml of anhydrous diethyl ether, and the mixture

was stirred for 3 days. The mixture was filtered, and the filtrate was washed with 15 ml of water in a separatory funnel. The organic phase was dried over magnesium sulfate and concentrated under reduced pressure, and the thick oily residue was subjected to column chromatography using hexane–ethyl acetate (20:1) as eluent.

Compound **V**. Yield 0.76 g (43%), bp 140–143°C (25 mm); published data [36]: bp 95 °C (0.5 mm). ^{13}C NMR spectrum (CS_2–CD_2Cl_2, 2:1), δ_C, ppm: at 25°C: 17.58 (C^1, C^7), 60.98 (C^2, C^6), 102.16 (C^4), 9.15 (C^8), 33.15 and 34.26 (C^9, $C^{9'}$), 23.47 (C^{10}, $C^{10'}$), 26.48 (C^{11}); at –85°C: 17.45 (C^1, C^7), 60.71 (C^2, C^6), 102.60 (C^4), 10.18 (C^8), 32.98 and 33.99 (C^9, $C^{9'}$), 23.53 (C^{10}, $C^{10'}$), 26.44 (C^{11}).

Compound **IV**. Yield 0.23 g (11%), colorless crystals, mp 59.8–61°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.53 m [10H, $(CH_2)_5$], 1.71 m (2H, CH), 3.53 t (CHCl, ^3J = 7.4 Hz), 4.13 m (4H, CH_2). ^{13}C NMR spectrum (CS_2–CD_2Cl_2, 2:1), δ_C, ppm: at 25°C: 26.38 (C^1, C^7), 57.73 (C^2, C^6), 103.17 (C^4), 39.97 (C^8), 34.02 and 34.26 (C^9, $C^{9'}$), 23.41, (C^{10}, $C^{10'}$), 22.14 (C^{11}); at –77°C: major conformer: 22.03 (C^1, C^7), 57.23 (C^2, C^6), 103.33 (C^4), 39.73 (C^8), 32.56 and 35.25 (C^9, $C^{9'}$), 23.44 and 23.57 (C^{10}, $C^{10'}$), 26.37 (C^{11}); minor conformer: 22.49 (C^1, C^7), 60.70 (C^2, C^6), 103.64 (C^4), 43.42 (C^8), 23.20 (C^{10}, $C^{10'}$), 25.61 (C^{11}). Found, %: C 61.08; H 8.08. $C_{11}H_{17}ClO_2$. Calculated, %: C 60.96; H 7.91.

***cis*-3,3-Dichlorocyclopropane-1,2-diyldimethanol (XIX).** A solution of 29.35 g (0.117 mol) of compound **III** in a mixture of 350 ml of THF and 250 ml of 0.1 N hydrochloric acid was kept for 12 days at room temperature. The solvent was distilled off under reduced pressure until a dark solid separated, and the precipitate was purified by column chromatography on silica gel using hexane–ethyl acetate (3:2) as eluent. Yield 16.3 g (81%), colorless crystals, mp 71–73°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.12 m (2H, CH), 2.58 s (2H, OH), 3.73 m (2H, CH_A), 4.40 m (2H, CH_B). Found, %: C 35.11; H 4.71. $C_5H_8Cl_2O_2$. Calculated, %: C 35.12; H 4.72.

***cis*-Cyclopropane-1,2-diyldimethanol (XX).** A solution of 2.03 g (11 mmol) of compound **V** in a mixture of 33 ml of THF and 23 ml of 0.1 N hydrochloric acid was kept for 12 days at room temperature. The solvent was distilled off under reduced pressure until a dark liquid residue was obtained, and the residue was subjected to column chromatography on silica gel using hexane–ethyl acetate (3:1) as eluent. Yield 0.81 g (73%), bp 73–75°C (0.5 mm); published data [36]: bp 103°C (1 mm). The ^{1}H NMR spectrum of the product was identical to that reported for an authentic sample [36].

4-*tert*-Butyl-8,8–dichloro-3,5-dioxa-4λ^5-phosphabicyclo[5.1.0]octane 4-oxide (XXI) (mixture of stereoisomers)**.** A solution of 2.54 g (16 mmol) of *tert*-butyldichlorophosphine in 10 ml of diethyl ether was added dropwise over a period of 10 min to a solution of 2.74 g (16 mmol) of compound **XIX** in a mixture of 40 ml of diethyl ether, 5 ml of methylene chloride, and 4.2 ml of triethylamine under stirring at 0°C. The mixture was then stirred for 5 h at room temperature, the precipitate of ammonium salt was filtered off, and the filtrate was concentrated under reduced pressure until grey crystals separated. According to the ^{31}P NMR data, the product was a mixture of diastereoisomers at a ratio of 11:1). By column chromatography on silica gel (chloroform–acetone, 20:1) we isolated 1.89 g (43%) of a mixture of isomeric phosphonates **XXI** as colorless crystals. Found, %: C 40.14; H 5.53. $C_9H_{15}Cl_2O_3P$. Calculated, %: C 39.58; H 5.54. The stereoisomers were separated be repeated chromatography. Minor isomer, mp 174–175°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.24 d (9H, CH_3, $^3J_{PH}$ = 16.9 Hz), 2.38 m (2H, CH), 4.57 m (4H, CH_2). ^{31}P NMR spectrum: δ_P 46.1 ppm. Major isomer, mp 100–102°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.22 d (9H, CH_3, $^3J_{PH}$ = 17.5 Hz), 2.39 m (2H, CH), 4.32 m (2H, 2-H_A, 6-H_A), 4.84 m (2H, 2-H_B, 6-H_B). ^{31}P NMR spectrum: δ_P 43.5 ppm.

4-Phenyl-3,5-dioxabicyclo[5.1.0]octane (XXII). *a*. A solution of 1.22 g (11.9 mmol) of diol **XX** and 1.04 g (9.79 mmol) of benzaldehyde in 30 ml of benzene containing a catalytic amount of *p*-toluenesulfonic acid was heated under reflux in a flask equipped with a Dean–Stark trap. The mixture was washed with a solution of sodium hydrogen carbonate and with water and dried over magnesium sulfate, and the solvent was distilled off under reduced pressure. Yield 1.83 g (98%), thick oil. The product was crystallized from hexane, mp 75–76°C. ^{13}C NMR spectrum (CCl_4), δ_C, ppm: 14.95 (C^8), 19.11 (C^1, C^7), 71.81 (C^2, C^6), 108.4 (C^4) (aromatic carbon signals are not given). Found, %: C 75.72; H 7.47. $C_{12}H_{14}O_2$. Calculated, %: C 75.76; H 7.42.

b. A zinc–silver couple was prepared by adding 9.9 g (151 mmol) of zinc to a hot solution of 0.06 g (0.359 mmol) of silver acetate in 60 ml of acetic acid. The obtained material was washed with anhydrous

diethyl ether, 95 ml of anhydrous diethyl ether and 0.05 g (0.464 mmol) of silver wire were added, and 5.9 g (22 mmol) of methylene iodide was then added dropwise. The mixture was stirred, and 10 g (56.7 mmol) of compound **XXIII** [37] was added from a dropping funnel over a period 15 min at room temperature to the Simmons–Smith reagent thus obtained. The mixture was heated for 20 h under reflux and cooled to 0°C, and 100 ml of diethyl ether and 7.5 ml of pyridine were added under vigorous stirring. The precipitate was filtered off, and the solvent was distilled off from the filtrate under reduced pressure to isolate 7.11 g (66%) of a thick oily material. Crystallization from hexane gave crystals with mp 75–76°C, which were identical to a sample prepared as described above in *a*.

REFERENCES

1. Vafina, R.M., Gubaidullin, A.T., Kataeva, O.N., Litvinov, I.A., Shtyrlin, Yu.G., and Klimovitskii, E.N., *Russ. J. Org. Chem*., 2006, vol. 42, p. 1563.
2. Pitea, D., Moro, G., and Favini, G., *J. Chem. Soc., Perkin Trans. 2*, 1987, p. 313.
3. Gianni, M.H., Gody, R., Asthana, M.R., Wursthorn, K., Patanode, P., and Kuivila, H.G., *J. Org. Chem*., 1977, vol. 42, p. 365.
4. Pilati, T. and Simonetta, M., *Cryst. Struct. Commun*., 1981, vol. 10, p. 265.
5. Klimovitskii, A.E., Zvereva, E.E., Chmutova, G.A., Dobrynin, A.V., Fedorenko, V.Yu., Shtyrlin, Yu.G., Litvinov, I.A., Bulygina, T.V., and Klimovitskii, E.N., *J. Mol. Struct*., 2007, vol. 828, p. 147.
6. Dumic, M., Vincovic, M., Filic, D., Jamnicky, B., Eskinja, M., and Kamenar, B., *J. Med. Chem*., 1995, vol. 38, p. 3034.
7. Prugovecki, B., Marinkovic, M., Vincovic, M., and Dumic, M., *Acta Crystallogr., Sect. E*, 2005, vol. 61, p. o2844; Tripathi, A.K., Bruhn, C., Flock, S., and Frauenrath, H., *Acta Crystallogr., Sect. C*, 2005, vol. 61, p. o705.
8. Gianni, M.H., Prezzavento, B., and Shea, K., *J. Org. Chem*., 1985, vol. 50, p. 1554.
9. Fedorenko, V.Yu., Baryshnikov, R.N., Khairutdinov, R.M., Vafina, R.M., Shtyrlin, Yu.G., Klochkov, V.V., and Klimovitskii, E.N., *Russ. J. Org. Chem*., 2005, vol. 41, p. 293.
10. Clark, G.R., Fraser-Reid, B., and Palenik, G., *J. Chem. Soc. D*, 1970, p. 1641.
11. Clark, G.R. and Palenik, G., *J. Chem. Soc., Perkin Trans. 2*, 1973, p. 194.
12. Soulier, J., Farines, M., Bonafos-Bastouil, A., and Laguerre, A., *Bull. Soc. Chim. Fr*., 1975, p. 1763.
13. Baryshnikov, R.N., Vafina, R.M., Fedorenko, V.Yu., Shtyrlin, Yu.G., and Klimovitskii, E.N., *Russ. J. Org. Chem*., 2003, vol. 39, p. 1029.
14. Taylor, K.G. and Chaney, J., *J. Am. Chem. Soc*., 1976, vol. 98, p. 4158.
15. Vafina, R.M., Kataeva, O.N., Litvinov, I.A., Sergeeva, G.N., and Klimovitskii, E.N., *Zh. Org. Khim*., 1993, vol. 29, p. 1885.
16. Talinli, E.N., Anac, O., and Kumbaraci, I.V., *Helv. Chim. Acta*, 2003, vol. 86, p. 2779.
17. Jendralla, H., *Chem. Ber*., 1982, vol. 115, p. 201.
18. Collado, I., Pedregal, C., Bueno, A.B., Marcos, A., Gonzalez, R., Blanco-Urgoiti, J., Perez-Castells, J., Schoepp, D.D., Wright, R.A., Johnson, B.G., Kingston, A.E., Moher, E.D., Hoard, D.W., Griffey, I., and Tizzano, J.P., *J. Med. Chem*., 2004, vol. 47, p. 456.
19. Baimashev, B.A., Fedorenko, V.Yu., Polozov, A.M., Shtyrlin, Yu.G., and Klimovitskii, E.N., *Russ. J. Org. Chem*., 2007, vol. 43, p. 911.
20. De Meijere, A., *Chem. Rev*., 2003, vol. 103, p. 931.
21. Greene, T.W. and Wuts, P.G.M., *Protective Groups in Organic Synthesis*, New York: Wiley, 1999, 3rd ed., p. 215.
22. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, J.A., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Cammi, R., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui, Q., Morokuma, K., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Baboul, A.G., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Gonzalez, C., Challacombe, M., Gill, P.M.W., Johnson, B.G., Chen, W., Wong, M.W., Andres, J.L., Head-Gordon, M., Replogle, E.S., and Pople, J.A., *Gaussian 98, Rev. A.7*, Pittsburgh PA: Gaussian, 1998.
23. Scott, A.P. and Radom, L., *J. Chem. Phys*., 1996, vol. 100, p. 16502.
24. Gavrilov, V.V., Dobrynin, A.B., Vafina, R.M., Klimovitskii, A.E., Fedorenko, V.Yu., Kataeva, O.N., Berdnikov, E.A., Litvinov, I.A., Shtyrlin, Yu.G., Fröhlich, R., and Klimovitskii, E.N., *J. Mol. Struct*., 2007, vol. 837, p. 79.
25. St-Amour, R. and St-Jacques, M., *Can. J. Chem*., 1983, vol. 61, p. 109.
26. Blanchette, A., Souriol-Lord, F., and St-Jacques, M., *J. Am. Chem. Soc*., 1978, vol. 100, p. 4055.
27. St-Amour, R. and St-Jacques, M., *Can. J. Chem*., 1981, vol. 59, p. 2283.

28. Arbuzov, B.A., Klimovitskii, E.N., Remizov, A.B., and Timirbaev, M.B., *Zh. Obshch. Khim*., 1981, vol. 51, p. 2705.
29. Klimovitskii, E.N., Timirbaev, M.B., and Arbuzov, B.A., *Zh. Obshch. Khim*., 1986, vol. 56, p. 144.
30. Seyferth, D., Yamazaki, H., and Alleston, D.L., *J. Org. Chem*., 1963, vol. 28, p. 703.
31. Vorogushin, A.V., Reshetova, M.D., Akhmedov, N.G., Ustynyuk, Yu.A., Eremenko, I.L., Nefedov, S.E., and Zinin, A.I., *Izv. Ross. Akad. Nauk, Ser. Khim*., 1998, p. 720.
32. Fedorinski, M., *Chem. Rev*., 2003, vol. 103, p. 1099.
33. Scholes, G. and Vietje, G., UK Patent Appl. no. 2088398, 1982.
34. Ashton, W.T., Meurer, L.C., Cantone, C.L., Field, A.K., Hannah, J., Karkas, J.D., Liou, R., Patel, G.F., Perry, H.C., Wagner, A.F., Walton, E., and Tolman, R.L., *J. Med. Chem*., 1988, vol. 31, p. 2304.
35. Grandjean, D., Pale, P., and Chuche, J., *Tetrahedron*, 1991, vol. 47, p. 1215.
36. Gajewski, J.J., Hawkins, C.M., and Jimenez, J.L., *J. Org. Chem*., 1990, vol. 55, p. 674.
37. Brannock, K.C. and Lappin, G.R., *J. Org. Chem*., 1956, vol. 21, p. 1366.