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From Simple Diols to Carbohydrate Derivatives of Phenylarsonic Acid

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A series of *spiro*-arsoranes bearing a phenyl moiety as the fifth substituent were synthesized applying open-chain, as well as cyclic vicinal diols, as chelating molecules by condensation reactions in aprotic solvents. The products synthesized are the *spiro* compounds of the general formula PhAs(DiolH$_{-2}$)$_2$ derived from the vicinal diols *meso*-2,3-butanediol, PhAs(*meso*-2,3-ButdH$_{-2}$)$_2$ (**1**), *exo-cis*-2,3-norbornanediol, PhAs{*exo-cis*-NobdH$_{-2}$}$_2$ (**2**), *cis*-1,2-cyclopentanediol, PhAs(*cis*-1,2-CptdH$_{-2}$)$_2$ (**3**), anhydroerythritol, PhAs(AnErythH$_{-2}$)$_2$ (**4**), *cis*-1,2-cyclohexanediol, PhAs(*cis*-1,2-ChxdH$_{-2}$)$_2$ (**5**), and *rac-trans*-1,2-cyclohexanediol, *rac*-{PhAs(*trans*-1,2-ChxdH$_{-2}$)$_2$} (**6**) which were identified as mononuclear compounds. A novel dimeric double-*spiro* environment for oxyarsoranes was found in the reaction products derived from the sterically demanding diols 1,1′-bicyclohexyl-1,1′-diol {PhAs(BhxdH$_{-2}$)O}$_2$ (**7**) and perfluorpinacol, {PhAs(FpinH$_{-2}$)O}$_2$ (**8**). The stability of the compounds in acidic and neutral aqueous media in the presence of organic co-solvents was investigated. A convenient synthetic procedure for *spiro*-oxyarsoranes, applying water as the solvent, was developed and proven to be advantageous. All of the compounds synthesized in this study were characterized by means of melting-point measurement, single-crystal X-ray analysis, NMR, IR, Raman, UV/vis, and mass spectrometry. The principles found for these reactions were valid for the methyl glycosides of β-D-ribofuranose and α-D-mannopyranose. The *spiro*-arsorane derived from methyl α-D-mannopyranoside, PhAs(Me-α-D-Man*p*2,3H$_{-2}$)$_2$ (**9**), is the first example of a structurally characterized carbohydrate-arsenic(V) compound.

Introduction

The biochemistry of silicon has been the subject of scientific research over the past decades.[1] Key questions in silicon metabolism stem from the low concentration of soluble forms of silicon. Orthosilicic acid, H_4SiO_4, for example, is stable in neutral aqueous solution only at concentrations around 1 mmol L^{-1}.[2] The question of controlled de- and repolymerization of silicic acid in organisms was sought to be answered by elucidation of the tentative role of various biomolecules as to whether these could act as cofactors forming intermediary silicon-containing compounds with increased solubility and sufficient hydrolytic stability. The majority of biomolecule-silicon compounds synthesized in this context are mononuclear pentacoordinate silicon chelates with mostly the anions of amino acids,[3] simple polyols,[4,5] hydroxycarboxylic acids,[3,6] and carbohydrates including the nucleosides.[7−12] Obtaining structural information about these compounds based on single-crystal X-ray analysis was hampered by gelation and amorphous precipitation encountered during efforts to grow crystals. The introduction of a phenyl moiety as the fifth

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(1) Christopher, Ch. T. G.; Kinrade, S. D *Stud. Plant Sci.* **2001**, *8*, 57–84.
(2) Holleman, A. F.; Wiberg, N. *Lehrbuch der Anorganischen Chemie*; Walter de Gruyter Verlag: Berlin-New York, 2007, p 959.
(3) Tacke, R.; Bertermann, R.; Burschka, Ch.; Dragota, S.; Penka, M.; Richter, I. *J. Am. Chem. Soc.* **2004**, *126*, 14493–14505.
(4) Kinrade, S. D.; Del Nin, J. W.; Schach, A. S.; Sloan, T. A.; Wilson, K. L.; Knight, C. T. G. *Science* **1999**, *285*, 1542–1545.
(5) Benner, K.; Klüfers, P.; Schuhmacher, J. *Z. Anorg. Allg. Chem.* **1999**, *625*, 541–543.
(6) Kinrade, S. D.; Hamilton, R. J.; Schach, A. S. *J. Chem. Soc., Dalton Trans.* **2001**, 961–963.
(7) Kinrade, S. D.; Deguns, E. W.; Gillson, A.-M. E.; Knight, C. T. G. *J. Chem. Soc., Dalton Trans.* **2003**, 3713–3716.
(8) Kinrade, S. D.; Balec, R. J.; Schach, A. S.; Wang, J.; Knight, C. T. G. *J. Chem. Soc., Dalton Trans.* **2004**, 3241–3243.
(9) Kästele, X.; Klüfers, P.; Kopp, F.; Schuhmacher, J.; Vogt, M. *Chem.—Eur. J.* **2005**, *11*, 6326–6346.
(10) Klüfers, P.; Kopp, F.; Vogt, M *Chem.—Eur. J.* **2004**, *10*, 4538–4545.
(11) Lambert, J. B.; Lu, G.; Singer, S. R.; Kolb, V. M. *J. Am. Chem. Soc.* **2004**, *126*, 9611–9625.
(12) Benner, K.; Klüfers, P.; Vogt, M. *Angew. Chem.* **2003**, *115*, 1088–1093; *Angew. Chem., Int. Ed.* **2003**, *42*, 1058−1062.

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ligand at the central silicon atom improved crystallizability, and several pentacoordinate carbohydrate-silicon complexes were characterized structurally.[10] These diffraction experiments proved silicon to be at the center of a *spiro* structure with the carbohydrate entities bonded to the central atom by way of five-membered diolato chelates.

The hydrolysis of the Si−O−C link in neutral aqueous solution, which becomes more dominant at lower pH values and higher dilution, has remained problematic, however.[9,12,13] Gaining structural and spectroscopic information about assumed silica-containing carbohydrate compounds in aqueous solutions at physiological pH values is thus hampered. A possible solution for this problem might be to shift the focus of research away from silicon toward another central atom that exhibits some degree of similarity. In terms of the diagonal-relationship concept, arsenic appears as a suitable silicon mimic. On the one hand, arsenic shows similarities to silicon: structural chemistry in its oxidation state +V, ability to form *spiro* compounds with diols and a phenyl moiety as the fifth ligand, and size according to uncorrected Shannon radii.[14,15] On the other hand, arsenic(V) acid does not share the major silicon-typical drawback of polycondensation. Additionally, pentavalent arsenicals are obtained as neutral molecules in contrast to anionic silicates. This enables the application of a broader range of solvents for synthesis, characterization, and crystallization without the need to search for appropriate counterions.

Early interest in the preparation of *spiro*-oxyarsoranes stemmed from medicinal chemistry. After the introduction of Salvarsan around 1910, arsenic-containing molecules attracted much attention during the first half of the 20th century and several arsenic-based drugs were introduced to the pharmaceutical agenda.[16] Research on this special field never ceased completely. Thus in 1986, a French patent described the preparation of a large variety of pentavalent *spiro*-arsoranes that were intended to show antiparasitic activity with substantially diminished toxicity.[17] A thorough characterization of the reaction products was not undertaken, however, the only physical constants reported being the melting points. Although the preparation of pentavalent *spiro*-arsoranes with a phenyl moiety has been known for more than 50 years, structural information about this class of molecules based on single X-ray diffraction experiments is scarce and predominantly limited to the comparison with the comparable phosphorus compounds.[18,19] Only the structures of the phenyl-substituted *spiro*-arsoranes derived from pinacol,[20] benzene-1,2-diol,[21] tolyl-1,2-diol[22] and ethane-1,2-diol, naphthalene-2,3-diol and 2-hydroxyisobutyric acid[23] have been reported so far.

Arsorane chemistry appears to be largely restricted to anhydrous conditions. Hence, most researchers avoid contact of arsoranes with water, which would be a serious restriction for the use of hydrophilic carbohydrate-derived substituents. In contrast to the common handling procedures, the Loiseau group exposed arylarsoranes to physiological media and found considerable life spans, though these substances rapidly hydrolyze at higher pH values.[24,25] The former finding is somewhat in contrast to claims from other authors.[18,26]

In this work we report on attempts to develop a carbohydrate-based arsorane chemistry. The focus is laid on the silicon−arsenic analogy.

Experimental Section

Phenylarsonic acid, *meso*-2,3-butanediol, (all Acros), ethylene glycol, benzene-1,2-diol, *rac-trans*-1,2-cyclohexanediol, *cis*-1,2-cyclohexanediol, methyl α-D-mannopyranoside (all Fluka), perfluoropinacol (ABCR), naphthalene-2,3-diol (Merck), *o*-aminophenol (EGA), *cis*-1,2-cyclopentanediol and pinacol (Aldrich) were obtained commercially and used as supplied without further purification. Anhydroerythritol,[27] 1,1′-bicyclohexyl-1,1′-diol,[28] *exo-cis*-2,3-norbornanediol,[29] and methyl β-D-ribofuranoside[30] were synthesized according to published procedures. Benzene and toluene (both Fluka) were dried over molecular sieves prior to use. The same holds true for the deuterated solvents ($CDCl_3$ and CD_3OD, both Aldrich) applied for NMR measurements. The synthesis of phenyl-substituted *spiro*-arsoranes derived from ethane-1,2-diol,[23] pinacol,[20] benzene-1,2-diol,[21] naphthalene-2,3-diol,[21] and *o*-aminophenol,[21] was conducted according to published procedures.

NMR spectra were recorded on a JEOL Eclipse 270, a JEOL Eclipse 400, and a JEOL EX-400 spectrometer. Data were processed using the Delta software (by JEOL). ^1H and ^{13}C NMR-signal shifts were referenced to TMS as primary internal or the solvent signal as secondary internal standard, $CFCl_3$ served as external reference for the shifts of ^{19}F signals. All measurements were performed at room temperature. Mass spectra were obtained on a JEOL JMS-700 apparatus and a Finnigan MAT 95 apparatus (HRMS). IR spectra were taken on a Perkin-Elmer Spectrum BX FT-IR spectrometer. Raman spectra were done on a Perkin-Elmer 2000 NIR FT-spectrometer. UV/vis spectra were recorded on a Varian CARY 50 BIO UV−visible spectrometer applying cuvettes made of quartz glass. Air was admitted in between the laser, the sample and the detector. Scanning was conducted between 1100 and 190 nm. Melting points were measured on a Büchi B-540 melting point apparatus and are uncorrected.

(13) Kästele, X.; Klüfers, P.; Tacke, R. *Angew. Chem.* **2006**, *118*, 3286–3288; *Angew. Chem., Int. Ed.* **2006**, *45*, 3212−3214.
(14) Shannon, R. D.; Prewitt, C. T. *Acta Crystallogr., Sect. B* **1969**, *25*, 925–946.
(15) Shannon, R. D. *Acta Crystallogr., Sect. A* **1976**, *32*, 751–767.
(16) Lloyd, N. C.; Morgan, H. W.; Nicholson, B. K.; Ronimus, R. S. *Angew. Chem.* **2005**, *117*, 963–966; *Angew. Chem., Int. Ed.* **2005**, *44*, 941−944.
(17) Wolf, J. G.; Madaule, Y.; Loiseau, P.; Gayral, P. *FR 2572730*, 1986.
(18) Salmi, E. J.; Merivuori, K.; Laaksonen, E. *Suomen Kemistilehti B* **1946**, *19*, 102–108.
(19) Mallon, T.; Wieber, M. *Z. Anorg. Allg. Chem.* **1979**, *454*, 31–34.
(20) Goldwhite, H.; Teller, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 5357–5362.
(21) Day, R. O.; Holmes, J. M.; Sau, A. C.; Holmes, R. R.; Deiters, J. A.; Devillers, J. R. *J. Am. Chem. Soc.* **1982**, *104*, 2127–2132.
(22) Fish, R. H.; Tannous, R. S. *Organometallics* **1982**, *1*, 1238–1240.
(23) Holmes, R. R.; Day, R. O.; Sau, A. C. *Organometallics* **1985**, *4*, 714–720.
(24) Rekik, L.; Loiseau, P.; Madaule, Y.; Tisnes, P.; Wolf, J.-G. *J. Chem. Res.* **1989**, 20–21.
(25) Loiseau, P. M.; Rekik, L.; Madaule, Y.; Gayral, P.; Wolf, J. G. *Arzneim.-Forsch.* **1993**, *43*, 1004–1009.
(26) Lederer, W. H. *Arsenic, Industrial, Biomedical Environmental Perspectives*; Van Nostrand Reinhold: New York, 1983.
(27) Otey, F. H.; Mehltretter, C. L. *J. Org. Chem.* **1961**, *26*, 1673.
(28) Corey, E. J.; Danheiser, R. L.; Chandrasekaran, S. *J. Org. Chem.* **1976**, *41*, 260–265.
(29) Wiberg, K. B.; Saegebarth, K. A. *J. Am. Chem. Soc.* **1957**, *79*, 2822–2824.
(30) Barker, J. R.; Fletcher, H. S. *J. Org. Chem.* **1961**, *26*, 4605–4609.

Table 1. Crystallographic Data for Compounds **1**−**9**

	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
empirical formula	$C_{14}H_{21}AsO_4$	$C_{20}H_{25}AsO_4$	$C_{16}H_{21}AsO_4$	$C_{14}H_{17}AsO_6$	$C_{18}H_{25}AsO_4$	$C_{18}H_{25}AsO_4$	$C_{36}H_{50}As_2O_6$	$C_{24}H_{10}As_2F_{24}O_6$	$C_{22}H_{32}AsNO_{12}$
M_r [g mol^{-1}]	328.23	404.32	352.25	356.20	380.30	380.30	728.60	1000.16	577.41
crystal system	monoclinic	orthorhombic	monoclinic	monoclinic	orthorhombic	monoclinic	monoclinic	triclinic	orthorhombic
space group	$P2_1/n$	*Pnma*	$P2_1$	$P2_1/c$	*Pbca*	$C2/c$	$P2_1/c$	$P\bar{1}$	$P2_12_12_1$
a [Å]	8.3864(2)	9.4010(2)	7.8018(1)	8.1666(1)	13.8522(1)	13.9281(3)	13.3869(11)	11.4842(2)	9.1751(6)
b [Å]	12.1694(3)	16.4780(4)	11.3880(2)	16.5853(3)	9.2574(1)	9.2826(2)	10.3562(7)	12.0072(2)	15.0294(10)
c [Å]	15.0855(4)	11.3090(2)	8.6949(2)	10.7640(2)	26.2408(2)	12.8324(3)	12.4204(10)	12.1719(2)	18.4998(11)
α [deg]	90	90	90	90	90	90	90	77.646(1)	90
β [deg]	102.734(1)	90	99.469(1)	104.441(1)	90	92.845(1)	105.514(5)	84.269(1)	90
γ [deg]	90	90	90	90	90	90	90	73.696 (1)	90
V [Å^3]	1501.72(7)	1751.87(6)	761.99(2)	1411.87(4)	3365.00(5)	1657.04(6)	1659.2(2)	1572.20(5)	2551.1(3)
Z	4	4	2	4	8	4	2	2	4
calc. density [g cm^{-3}]	1.452	1.533	1.535	1.676	1.501	1.525	1.458	2.113	1.503
μ [mm^{-1}]	2.271	1.963	2.243	2.433	2.038	2.070	2.059	2.310	1.396
Flack parameter			−0.003(9)						−0.014(8)
$R(F_{obs})$	0.0386	0.0321	0.0260	0.0339	0.0257	0.0291	0.0421	0.0295	0.0350
$R_w(F^2)$	0.0743	0.0847	0.0593	0.0808	0.0697	0.0725	0.0709	0.0711	0.0841
S	1.017	1.041	1.047	1.030	1.037	1.106	0.752	1.047	0.978

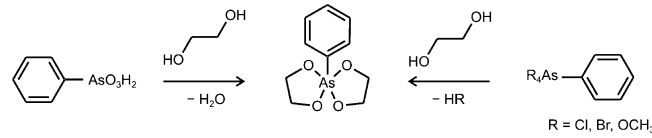
Unless otherwise stated all manipulations and reactions were conducted without special precautions to exclude oxygen or moisture. Elemental analysis were precluded by technical problems arising from arsenic in the sample resulting in severe damage to the analytical apparatus. The application of benzene as the solvent during the synthetic procedures is not mandatory but can also be substituted for toluene or cyclohexane.

Preparation of and analytical data for compound **1** are described in detail, for synthesis and analytical data of compounds **2**−**9**, see Supporting Information.

PhAs(meso-ButdH$_{-2}$)$_2$ (1). Phenylarsonic acid (1.01 g, 5 mmol) and *meso*-2,3-butanediol (0.90 g, 10.0 mmol) were suspended in benzene (50 mL) and heated under reflux for 4 h. The water liberated during the reaction was removed by azeotropic distillation and collected in a Dean−Stark trap. The solvent was removed entirely from the clear reaction mixture under reduced pressure, and the oily residue was stored at ambient temperature. In the course of 2 months the oil completely crystallized yielding colorless platelets with a slightly sweet odor (1.56 g, 4.75 mmol, 95.0% yield). ^{1}H NMR ($CDCl_3$, 399.8 MHz, 22 °C): δ = 8.24−8.22 (m, H_{ar}), 8.08−8.05 (m, H_{ar}), 7.97−7.93 (m, H_{ar}), 7.56−7.45 (m, H_{ar}), 4.24−4.14 (m, HCO), 3.91−3.77 (m, HCO), 3.62−3.57 (m, HCO), 1.21−1.18 (m, CH_3), 1.06−1.04 (m, CH_3), 1.00−0.99 (m, CH_3) ppm. ^{13}C{^{1}H} NMR ($CDCl_3$, 100.5 MHz, 24 °C): δ = 138.8 (C_{ar}), 137.8 (C_{ar}), 135.5 (C_{ar}), 133.5 (C_{ar}), 132.4 (C_{ar}), 132.2 (C_{ar}), 132.1 (C_{ar}), 131.6 (C_{ar}), 129.2 (C_{ar}), 129.1 (C_{ar}), 129.0 (C_{ar}), 128.9 (C_{ar}), 70.4 (HCO), 70.3 (HCO), 69.2 (HCO), 69.1 (HCO), 16.5 (CH_3), 16.1 (CH_3) ppm. MS-EI$^+$ (intensity): m/z = 328 (0.5, [M]$^+$), 152 (98, [M − $C_4H_8O_2$ − $C_4H_8O_2$]$^+$). HRMS-DEI$^+$: calculated for $C_{14}H_{21}AsO_4^+$ (M^+): 328.0656; found: 328.0647. IR absorptions (neat): νbar = 3059 (w), 2982 (w), 2972 (w), 2920 (w), 2873 (w), 1455 (w), 1437 (m), 1375 (m), 1354 (w), 1344 (w), 1305 (w), 1287 (w), 1261 (w), 1166 (w), 1111 (w), 1075 (s), 1013 (s), 995 (m), 938 (m), 920 (s), 910 (s), 887 (w), 791 (s), 752 (s), 706 (s), 696 (s), 680 (s), 665 (s), 634 (s) cm^{-1}. Raman frequencies (100 mW, 100 scans) (intensity): 3062 (57), 2986 (44), 2973 (33), 2938 (52), 2920 (77), 2874 (27), 1578 (19), 1461 (10), 1445 (19), 1350 (7), 1323 (9), 1291 (12), 1172 (14), 1160 (17), 1142 (7), 1113 (9), 1089 (10), 1017 (18), 1000 (71), 795 (12), 689 (11), 666 (100), 638 (7), 615 (13), 599 (14), 521 (9), 432 (10), 342 (51), 283 (14), 245 (22). UV/vis (acetonitrile): λ_{max}/nm = 258, 263, 269, UV/vis (cyclohexane): λ_{max}/nm = 258, 264, 271. Melting point: 60.9−64.9 °C.

Crystal Structure Determination and Refinement. Crystals suitable for X-ray crystallography were selected by means of a polarization microscope, mounted on the tip of a glass fiber and investigated on a Nonius KappaCCD diffractometer using graphite-monochromatized Mo Kα radiation (λ = 0.71073 Å) except compounds **7** and **9** which were investigated on a Stoe IPDS diffractometer or an Oxford Xcalibur diffractometer, respectively, using the same type of radiation. All investigations were conducted at a temperature of 200(2) K. The structures were solved by direct methods (SIR 97, SHELXS) and refined by full-matrix least-squares calculations on F^2 (SHELXL-97). Anisotropic displacement parameters were refined for all non-hydrogen atoms. The number of restraints given refers to ISOR and DFIX restraints. Crystallographical data are collected in Table 1. CCDC 654409 (**1**), 654410 (**2**), 654411 (**3**), 654412 (**4**), 654413 (**5**), 654414 (**6**), 654416 (**7**), 654417 (**8**), 654418 (**9**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

Scheme 1. Pathways for the Preparation of *spiro*-Oxyarsoranes



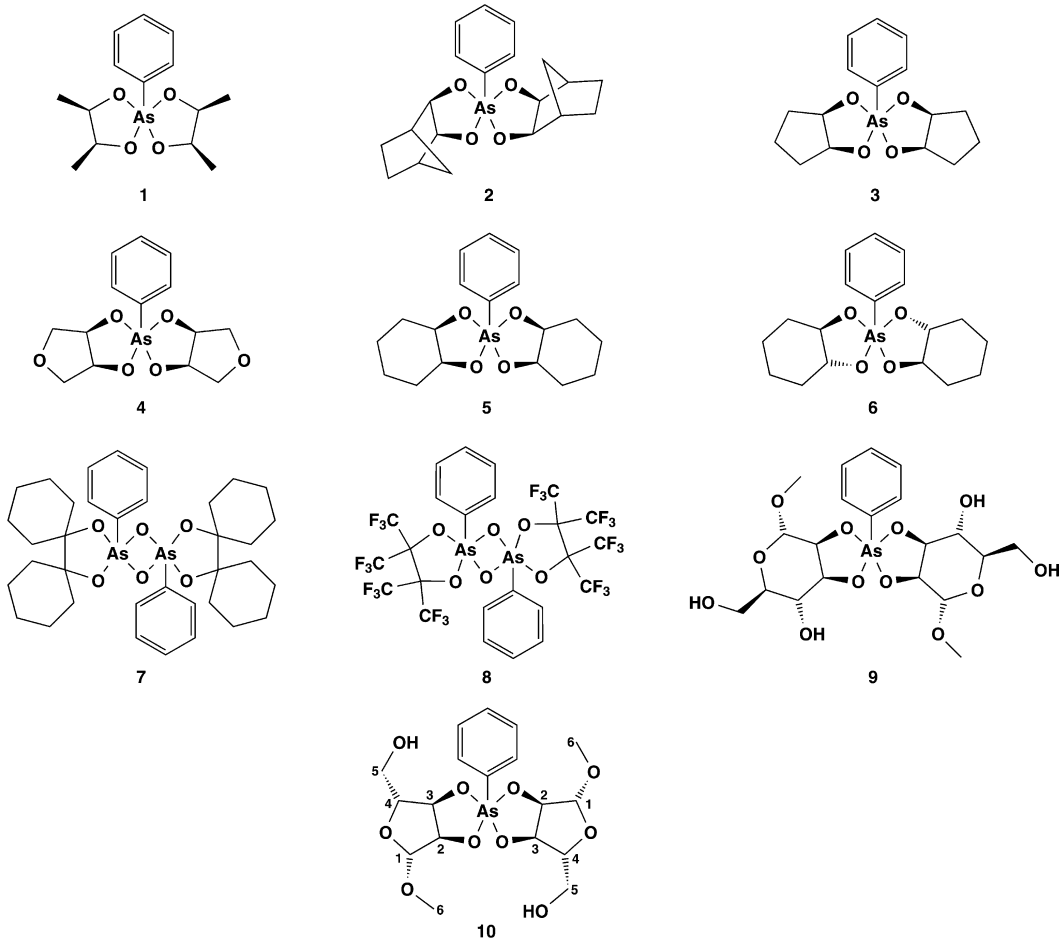
Results and Discussion

Diol-derived *spiro*-arsoranes bearing a phenyl moiety as the fifth ligand may be prepared by two different synthetic protocols found in the literature (Scheme 1):

In a first approach, Dale and Frøyen prepared *spiro*-arsoranes derived from simple and aromatic diols by reacting pentavalent phenylarsoranes endowed with four easily substitutable groups such as chloro, bromo, or methoxy substituents with the diols to gain the desired products by stepwise substitution reactions.[31] A second approach was introduced by Salmi, Merivuori, and Laaksonen which utilizes phenylarsonic acid that was condensed with 2 equiv of the same diols as used by Dale and Frøyen and a couple of α-hydroxycarboxylic acids with subsequent azeotropic removal of the water liberated during the reaction.[18] To prevent the rather cumbersome preparation and handling of the moisture-sensitive pentavalent phenylarsoranes, the sec-

(31) Dale, A. J.; Frøyen, P. *Acta Chem. Scand. B* **1975**, *29*, 741–748.

Scheme 2. *spiro*-Arsoranes in This Study



ond route was applied throughout this work. The starting material, phenylarsonic acid, is a commercially available, easy-to-handle compound. Following this synthetic approach, we prepared the compounds depicted in Scheme 2.

***syn/anti* Isomerism.** A particularly typical property of carbohydrate-derived *spiro*-silicates is *syn*/*anti* isomerism. Since a carbohydrate's diol functions usually lack C_2 symmetry, the relative orientation of the diol's substituents with respect to the fifth substituent on the pentacoordinate center gives rise to this type of isomerism. Both the simple diols used in prior work, ethane-1,2-diol and its tetramethyl derivative pinacol, however, can form C_2-symmetric chelate rings and lack *syn*/*anti* isomerism intrinsically. To check for the significance and spectroscopic characteristics of *syn*/*anti* isomers, the starting point of this investigation thus was the condensation of phenylarsonic acid with *meso*-2,3-butanediol (*meso*-Butd), the C_s-symmetric dimethyl derivative of ethane-1,2-diol. Assignment of ^{13}C NMR signals to the different isomers was done by analogy to the corresponding phenyl silicates.[9]

^{13}C NMR spectra of redissolved crystals of the reaction product PhAs(*meso*-ButdH$_{-2}$)$_2$ (**1**) showed the expected characteristics of *syn*/*anti* isomerism. Particularly indicative were two pairs of signals for the carbon atoms bound to the oxygen atoms: one pair is made from a single small signal of the C_{2v}-symmetric *syn*/*syn* isomer and a larger signal of the *syn* component of the C_s-symmetric *syn*/*anti* isomer; the other pair stems from the *anti* component of the *syn*/*anti* isomer and, giving rise to the largest signal, the C_{2v}-symmetric *anti*/*anti* major isomer (compare Figure 9 in the carbohydrate chapter). The molar ratios of the isomers roughly correspond to 2:3:1 for *syn*/*anti*, *anti*/*anti*, and *syn*/*syn* in terms of ^{13}C NMR signal intensities. This situation is mirrored by other signals. Figure 9 shows the typical 3-fold split of the ^{13}C NMR signal of each of the phenyl carbon atoms (because of accidental signal overlap in the *ortho*/*para* range, the signals of the *meta* region are depicted). The behavior of **1** is typical for all the compounds of this work: on the one hand, *syn*/*anti* isomerism is manifest on the NMR time scale and thus dominates the clearly resolved spectra. On the other hand, isomeric equilibrium adjusts so fast that redissolved crystals of a pure isomer yield the spectra of the equilibrium mixture immediately after dissolution. Being a rule throughout this work, the major component of the reaction mixture is found in the solid state. Accordingly, structural analysis on crystals of **1** reveals the *anti*/*anti* isomer (Figure 1). It should be noted that, because of rapid equilibration of the solution both on redissolution of crystals and precipitation of solid, the yield of solid product exceeds the amount of the respective isomer at equilibrium. The conformation of the molecules of **1** corresponds to a square pyramid which is distorted along the Berry pseudorotation coordinate to 36% toward a trigonal bipyramid. Bond distances, angles, and torsional angles are settled around the

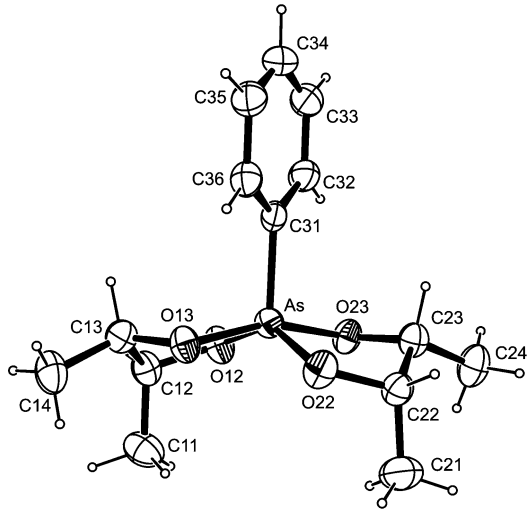


Figure 1. Molecular structure of PhAs(*meso*-2,3-ButdH$_{-2}$)$_2$ in crystals of **1** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O22 1.782(2), O12 1.783(2), O23 1.800(2), O13 1.804(2), C31 1.919(3); O22−As−O12 139.85(9), O22−As−O23 88.42(7), O12−As−O23 84.36(8), O22−As−O13 84.98(7), O12−As−O13 88.42(7), O23−As−O13 159.78(8), C12−O12−As 113.3(1), C13−O13−As 109.6(1), C22−O22−As 113.5(1), C23−O23−As 109.0(1); torsion angles [deg]: O12−C12−C13−O13 41.0(3), O22−C22−C23−O23 38.6(3); puckering analysis: As−O12−C12−C13−O13 Q_2 = 0.383(2) Å, φ_2 = 290.7(3)°, envelope on C13, As−O22−C22−C23−O23 Q_2 = 0.387(2) Å, φ_2 = 299.3(3)°, twisted on C23−O23.

values reported in the literature for the corresponding structures with ethylene glycol and pinacol.[23,20] On attempts to determine the melting point of crystals of **1**, the issue of *syn/anti* isomerism again becomes evident. Despite the fact that spirocyclic phenylarsoranes are thermally stable and may be molten and resolidified repeatedly, a sharp melting point is observed for C_2-symmetric alkylenedioxy substituents only, for example, in the case of *trans*-1,2-cyclohexanediol, whereas broader softening intervals are observed for the other substituents.

One parameter that determines the molar ratio of the three isomers is the steric bulk on each of the hemispheres around the diol function. When dissolved crystals of the condensation product of phenylarsonic acid and *exo-cis*-norbornanediol, PhAs{*exo-cis*-NobdH$_{-2}$}$_2$ (**2**), are investigated by means of ^{13}C NMR spectroscopy, the characteristic number of resonances is observed. Yet, the signals' intensities for corresponding carbon atoms show the clear predominance of the *anti*/*anti* isomer in solution (about 1:5:0.2 for *syn*/*anti*, *anti*/*anti*, and *syn*/*syn*). The structure of the C_s-symmetric molecules of the *spiro*-arsorane **2** in the solid state is shown in Figure 2. The arsenic atom is found distorted square-pyramidal (sp, 29% along the Berry pseudorotation coordinate toward trigonal-bipyramidal [tbp]). The rigid bicyclic framework of the diol-derived substituent is present in an overall eclipsed arrangement.

Basic Carbohydrate Chelation Patterns: Cyclic Diols. In a step toward carbohydrate derivatives of arsenic(V), some cyclic vicinal diols were investigated that model the established metal-binding sites of a carbohydrate: the *cis*-furanose, the *cis*-pyranose, and the *trans*-pyranose. The steric requirements for furanose binding are modeled by *cis*-1,2-cyclopentanediol (*cis*-Cptd). Reaction with phenylarsonic acid yields PhAs(*cis*-CptdH$_{-2}$)$_2$ (**3**). Crystal-structure analysis proves the presence of a *spiro*-arsorane in the solid state (Figure 3). The configuration is *syn*/*anti*, the conformation at the arsenic center is intermediate between sp and tbp (sp, distorted to 39% toward tbp on the *Berry* pseudorotation coordinate). The chelate rings are flat (compare the diol torsion angles and the puckering amplitudes in Figure 3), in agreement with the small size of the arsenic central atom and the conformational flexibility of the five-membered cyclopentane ring. The *syn*/*anti* arrangement of the cyclopentylenedioxy substituents with respect to the

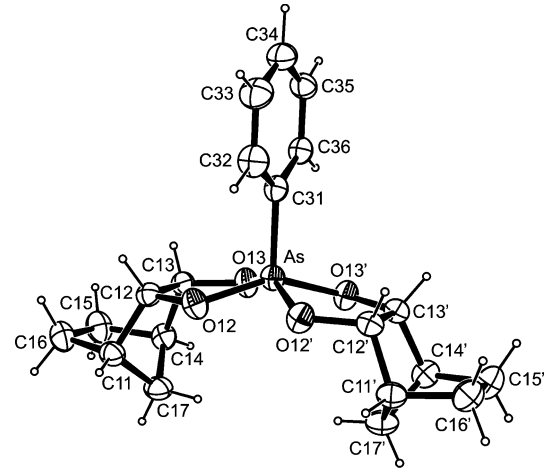


Figure 2. Structure of the C_s-symmetric molecules of PhAs{*exo-cis*-NobdH$_{-2}$}$_2$ in crystals of **2** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O13 1.790(2), O12 1.796(2), C31 1.908(3); O13−As−O13′ 82.9(1), O13−As−O12′ 149.31(7), O13−As−O12 88.59(7), O13′−As−O12 149.31(7), O12′−As−O12 83.9(1), C12−O12−As1 113.9(1), C13−O13−As 114.7(1); torsion angle [deg]: O12−C12−C13−O13 2.4(2); puckering analysis: As−O12−C12−C13−O13 Q_2 = 0.228(2) Å, φ_2 = 185.3(5)°, envelope on As.

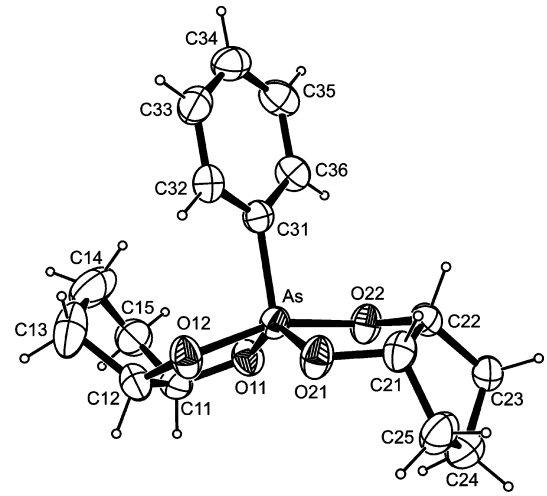


Figure 3. Molecular structure of PhAs(*cis*-1,2-CptdH$_{-2}$)$_2$ in crystals of **3** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O11 1.778(2), O21 1.779(2), O22 1.801(2), O12 1.802(1), C31 1.918(3); O11−As−O21 138.40(9), O11−As−O22 84.27(8), O21−As−O22 88.06(8), O11−As−O12 88.57(7), O21−As−O12 84.78(9), O22−As−O12 159.8(1), C11−O11−As 116.1(2), C12−O12−As 115.5(1), C21−O21−As 115.3(2), C22−O22−As 113.1(2); torsion angles [deg]: O11−C11−C12−O12 −3.3(4), O21−C21−C22−O22 −13.7(3); puckering analysis of the chelate rings: As−O11−C11−C12−O12 Q_2 = 0.106(2) Å, φ_2 = 165(2)°, twisted on O12−As, As−O21−C21−C22−O22 Q_2 = 0.253(2) Å, φ_2 = 151.6(5)°, envelope on O22.

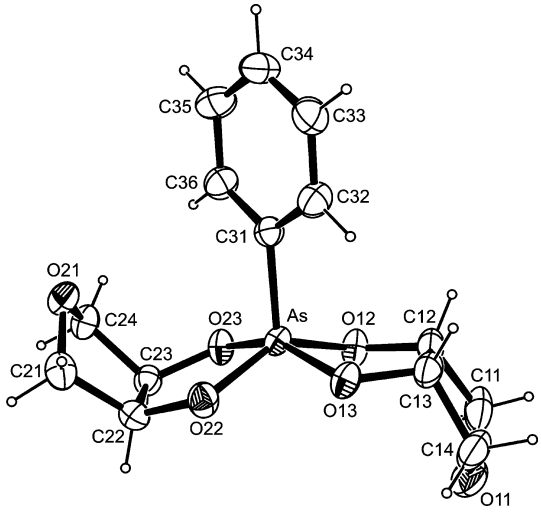


Figure 4. Molecular structure of PhAs(AnErytH$_{-2}$)$_2$ in crystals of **4** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O22 1.783(2), O12 1.791(2), O23 1.792(2), O13 1.805(2), As−C31 1.918(3); O22−As−O12 141.98(9), O22−As−O23 88.29(8), O12−As−O23 83.17(7), O22−As−O13 84.35(8), O12−As−O13 87.66(8), O23−As−O13 154.44(8), C12−O12−As 113.6(2), C13−O13−As 113.7(2), C22−O22−As 116.4(2), C23−O23−As 116.3(2); torsion angles [deg]: O12−C12−C13−O13 −4.3(3), O22−C22−C23−O23 1.3(3); puckering analysis: As−O12−C12−C13−O13 $Q_2 = 0.275(2)$ Å, $\varphi_2 = 8.0(6)°$, envelope on As, As−O22−C22−C23−O23 $Q_2 = 0.085(2)$ Å, $\varphi_2 = 353(2)°$, envelope on As.

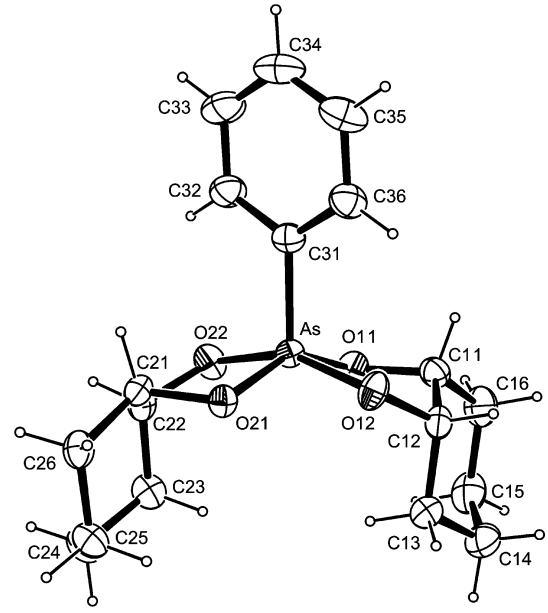


Figure 5. Molecular structure of PhAs(*cis*-1,2-ChxdH$_{-2}$)$_2$ in crystals of **5** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O11 1.799(1), O21 1.801(1), O12 1.805(1), O22 1.810(1), C31 1.921(2); O11−As−O21 146.51(5), O11−As−O12 88.38(5), O21−As−O12 84.57(5), O11−As−O22 84.79(5), O21−As−O22 88.34(5), O12−As−O22 155.69(6), C11−O11−As 110.2(1), C12−O12−As 112.14(9), C21−O21−As 109.93(9), C22−O22−As 112.30(9); torsion angles [deg]: O11−C11−C12−O12 44.9(2), O21−C21−C22−O22 44.0(2); puckering analysis: As−O11−C11−C12−O12 $Q_2 = 0.401(2)$ Å, $\varphi_2 = 259.7(2)°$, envelope on C11, As−O21−C21−C22−O22 $Q_2 = 0.400(2)$ Å, $\varphi_2 = 254.9(2)°$, envelope on C21.

phenyl moiety in the solid state corresponds to the relative concentrations of the three expected isomers in solution, the *syn*/*anti* isomer being the major solution species (compare Figure 9).

In terms of acidity, the C_s-symmetric oxa analog of cyclopentane-1,2-diol, anhydroerythritol (AnEryt), is closer to a furanose than the carbocyclic diol.[9,32] The reaction of phenylarsonic acid with anhydroerythritol yielded the condensation product PhAs(AnErytH$_{-2}$)$_2$ (**4**). Crystal structure analysis showed the *meso*-oxolane rings in a nearly perfect eclipsed atomic arrangement, both rings adopting an envelope conformation with the oxygen atoms outside the plane (Figure 4). The coordination geometry around arsenic is distorted sp with a value of 24% toward tbp along the Berry pseudorotation coordinate. The *syn*/*anti* orientation of the *meso*-oxolane rings is in agreement with the one found in the crystal structure of **3**. Correspondingly, ^{13}C NMR spectra of **4** show a picture comparable to the spectra of **3**: two groups of resonances are observed, the one at higher field consisting of three signals (with one showing slight broadening). The group at lower field is composed of four distinct signals. Again, the *syn*/*anti* isomer is the major species in the reaction mixture.

The *cis*-pyranose mode of carbohydrate bonding was modeled with *cis*-1,2-cyclohexanediol (*cis*-1,2-Chxd). Following the standard procedure, a crystalline sample of PhAs(*cis*-1,2-ChxdH$_{-2}$)$_2$ (**5**) was obtained whose structure was elucidated by means of X-ray analysis (Figure 5). The two cyclohexane rings adopt a chair conformation, the overall configuration is *anti*/*anti*. The coordination polyhedron shows only a low degree of distortion: the conformation of the arsenic atom is sp, slightly distorted toward tbp (17% on the Berry path). The ^{13}C NMR spectrum of redissolved crystals of **5** indicates *syn*/*anti* isomerism.

Because of an unsuitably large torsion angle, a *trans*-furanose has never been observed as a chelate-forming entity. Accordingly, phenylarsonic acid and *trans*-1,2-cyclopentanediol yielded no defined reaction product even after prolonged heating periods, the removal of solvent invariably resulting in the formation of oily, viscous liquids, whose ^{13}C NMR spectra showed only a multitude of signals in the aromatic and aliphatic region. This can be interpreted in terms of the lack of a single stable product such as a chelate. Instead, oligonuclear species may have been formed as has been found with silicon.[9]

Silicates also have not been found chelated by *trans*-pyranoidic diols. The reaction of racemic *trans*-1,2-cyclohexanediol (*trans*-1,2-Chxd) with phenylarsonic acid, however, yielded crystalline *rac*-{PhAs(*trans*-1,2-ChxdH$_{-2}$)$_2$} (**6**) whose structure is depicted in Figure 6. The coordination geometry in **6** is essentially tbp with a value of only 17% on the Berry pseudorotation coordinate toward sp. The bond length along the bipyramid's axis (1.84 Å) is found to be slightly elongated with respect to other *spiro*-oxyarsoranes in the solid state. The diol torsion angle, O−C−C−O, is compressed to about 45°. ^{13}C NMR spectra of redissolved crystals of **6** show three groups of signals consisting of four signals each for every carbon atom in the cyclohexane ring. Each of the two groups at lower field are divided into signal

(32) Burchard, W.; Habermann, N.; Klüfers, P.; Seger, B.; Wilhelm, U. *Angew. Chem.* **1994**, *106*, 936–939; *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 884−887.

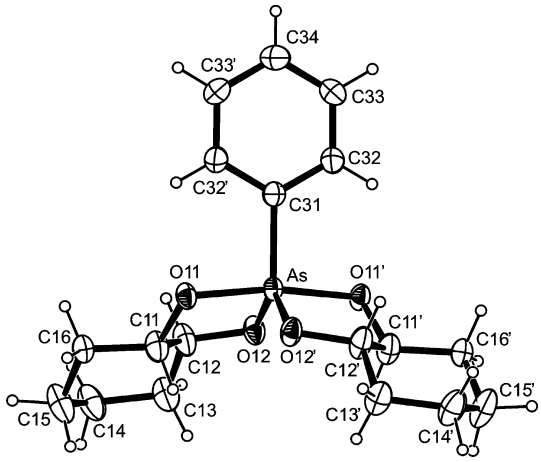


Figure 6. Structure of the C_2-symmetric molecules of *rac*-{PhAs(*trans*-1,2-ChxdH$_{-2}$)$_2$} in crystals of **6** (50% probability ellipsoids); the (*S*,*S*)-configured enantiomer is depicted. Distances [Å] and bond angles [deg]: from As to O12 1.780(1), O11 1.837(1), C31 1.928(3); O12−As−O12′ 122.5(1), O12−As−O11′ 86.44(6), O12−As−O11 88.83(6), O11′−As−O11 170.16(9), C11−O11−As 108.3(1), C12−O12−As 111.7(1); torsion angles [deg]: O11−C11−C12−O12 44.8(2); puckering analysis: As−O11−C11−C12−O12 Q_2 = 0.388(2) Å, φ_2 = 258.8(2)°, envelope on C11. The all-*S*-configured isomer is shown.

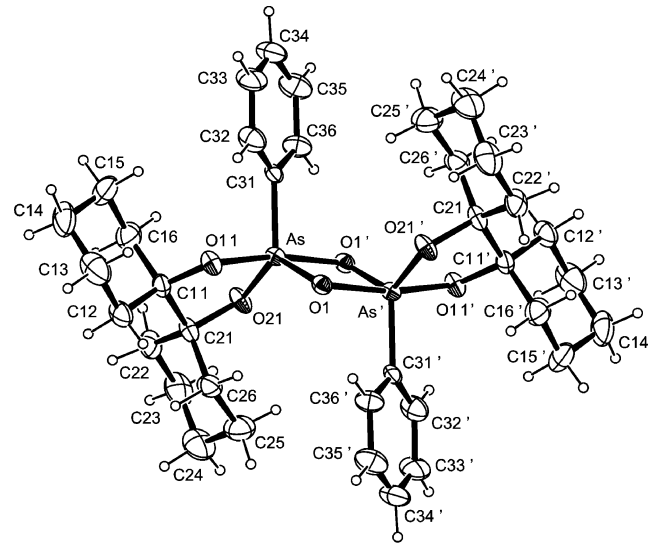


Figure 7. Structure of the C_s-symmetric molecules of {PhAs(BhxdH$_{-2}$)O}$_2$ in crystals of **7** (80% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O1 1.727(3), O21 1.763(2), O11 1.808(2), C31 1.905(3), O1′ 1.916(3); As′···As 2.7569(7); O1−As−O21 122.5(1), O1−As−O11 93.2(1), O21−As−O11 89.3(1), O1−As−O1′ 81.8(1), O21−As−O1′ 86.4(1), O11−As−O1′ 170.3(1), As−O1−As′ 98.2(1), C11−O11−As 111.8(2), C21−O21−As 112.1(2); torsion angles [deg]: O11−C11−C21−O21 −43.8(3); puckering analysis: As−O11−C11−C21−O21 Q_2 = 0.398(4) Å, φ_2 = 89.2(3)°, twisted on C11−C21.

pairs of equal intensity. The occurrence of two distinct species is not unexpected since the diol was used as a racemic mixture. Using the abbreviations *r* = (1*R*,2*R*) and *s* = (1*S*,2*S*), the *rr* and the *ss* isomer make up the solid exclusively. On dissolution, the *meso* (*rs*) isomer obviously forms in addition to the enantiomers. It should be noted that *syn*/*anti* isomerism in solution requires at least breaking one bond in the chelate rings and may be formulated as an intramolecular process. Isomerism between chiral and *meso* forms, however, requires diol scrambling between different arsorane molecules, which obviously is possible even under the mild reaction conditions applied.

Preventing Bis-Chelation: Sterically Demanding Diols. Having established the basic rules for the possible interaction between arsenic and carbohydrates on the basis of simple diols that model characteristic features of sugars, it seemed of interest to shed light on the chelating abilities of sterically more demanding ligands. 1,1′-Bicyclohexyl-1,1′-diol (Bhxd) was considered to be an appropriate candidate for this task by offering two hydroxy groups residing on two different but interconnected cyclohexane ring systems. The composition of the condensation product {PhAs(BhxdH$_{-2}$)O}$_2$ (**7**) turned out different from the compounds described so far. Upon cooling to room temperature platelike crystals were retrieved from the reaction mixture. The molecular structure is depicted in Figure 7. It shows a dimeric *spiro*-oxyarsorane with two interconnected *spiro* substructures, a coordination mode only reported once for an aza analog with bridging imido functions.[33] A prominent structural feature is a four-membered ring composed of alternating arsenic and oxygen atoms. Every arsenic atom is bound in a chelating mode to one 1,1′-bicyclohexyl-1,1′-enedioxy fragment. The fifth position on each arsenic atom is occupied by a phenyl moiety reaching above and below the plane spanned by the central four-membered ring. The central ring itself adopts the outward appearance of a rhombus narrowing on the arsenic atoms. The As−O distances are measured at values of close to 1.73 Å and 1.92 Å, the highest value for *spiro*-oxyarsoranes in the solid state so far. The distances between the oxygen atoms of the diol and arsenic are settled around typical values of about 1.76 Å for the equatorial oxygens and about 1.81 Å for the oxygen atoms connecting by way of an axial position. The cyclohexane rings in the substituents are present in the chair conformation. The dihedral angle of about 44° along the O−C−C−O moiety is due to an intra-residue staggered arrangement of the two cyclohexane rings.

Reacting perfluoropinacol (Fpin) as another bulky diol with phenylarsonic acid corroborates these findings. The progress of reaction and crystallization resembles much the synthesis of **7**: after cooling to room temperature crystals of {PhAs(FpinH$_{-2}$)O}$_2$ (**8**) settled out of the reaction mixture. The results of diffraction experiments shown in Figure 8 proved the synthesis of a second structure closely resembling the one of **7** in terms of bond lengths and angles. Unlike the situation found for the molecular structure of **7**, the connection between the two arsenic-containing building blocks in **8** is realized by an oxygen atom settled in the equatorial plane of the two trigonal-bipyramidal substructures and one oxygen atom residing in the axial position of both trigonal-bipyramidal substructures. The bulky CF_3 groups in the terminally bonded ligands are found in an overall staggered conformation. Both **7** and **8** form at the 2:1 molar ratio of diol and As precursor, as well as at the stochiometric 1:1 ratio, where no unreacted phenylarsonic acid is present in the crude

(33) Kokorev, G. I.; Litvinov, I. A.; Musin, R. Z.; Naumov, V. A. *Russ. J. Gen. Chem.* **1991**, *61*, 2518–2526; *Zhur. Obsh. Khim.* **1991**, *61*, 2713−2721.

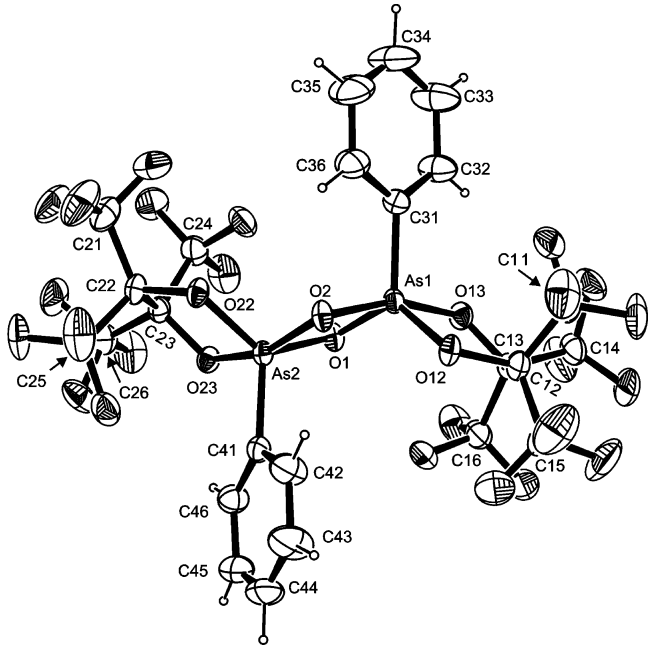


Figure 8. Molecular structure of $\{PhAs(FpinH_{-2})O\}_2$ in crystals of **8** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As1 to O1 1.786(1), O12 1.793(1), O2 1.804(1), O13 1.840(2), C31 1.898(2); from As2 to O1 1.787(1), O2 1.794(1), O22 1.799(1), O23 1.838(1), C41 1.898(2); As1···As2 2.7009(3); O1−As1−O12 125.88(7), O1−As1−O2 82.11(6), O12−As1−O2 86.73(6), O1−As1−O13 88.78(6), O12−As1−O13 85.85(6), O2−As1−O13 161.72(7), O1−As2−O2 82.36(6), O1−As2−O22 128.99(7), O2−As2−O22 86.34(6), O1−As2−O23 88.25(6), O2−As2−O23 160.01(7), O22−As2−O23 85.93(6), As1−O1−As2 98.23(7), As2−O2−As1 97.30(7), C12−O12−As1 117.0(1), C13−O13−As1 115.3(1), C22−O22−As2 116.5(1), C23−O23−As2 115.1(1); torsion angles [deg]: O12−C12−C13−O13 −35.7(2), O22−C22−C23−O23 −36.9(2); puckering analysis: As1−O12−C12−C13−O13 Q_2 = 0.325(2) Å, φ_2 = 96.0(3)°, twisted on C12−C13, As2−O22−C22−C23−O23 Q_2 = 0.334(2) Å, φ_2 = 94.1(2)°, twisted on C22−C23.

reaction product. When anhydroerythritol was reacted with an equimolar amount of phenylarsonic acid, no dinuclear compound formed; instead, mononuclear **4** was obtained. Thus, obviously, the binuclear motif is less stable than a mixture of mononuclear *spiro*-arsorane and phenylarsonic acid (including its condensation products) and is formed only when the *spiro* compound is distinctly destabilized by steric strain.

1,3- vs 1,2-Alkylenedioxy Binding. So far reactions between phenylarsonic acid and vicinal diols were conducted. In the corresponding reaction products the central atom was always part of a five-membered ring. For a carbohydrate, six-membered chelate structures have to be taken into account as well. For silicon, a variety of compounds is known for various coordination numbers, and at least one tetracoordinate *spiro* compound with an aromatic 1,3-diol was characterized by means of single crystal X-ray analysis.[34] Few examples with analogous structures containing arsenic are described and have been characterized only by means of NMR and IR spectroscopy.[31,35] As of today, no solid state structure of a *spiro* compound derived from phenylarsonic acid and a 1,3-diol based on single crystal X-ray analysis is apparent in the literature. The reaction between 1,3-propanediol, 2,2-dimethyl-1,3-propanediol and *cis*-1,3-cyclopentanediol by the standard procedure applied throughout this work yielded only oily, viscous products whose ^{13}C NMR spectra showed the presence of more than one species in the reaction mixture. Repeating the reactions in the absence of benzene by suspending phenylarsonic acid in neat diols and subsequent heating resulted in clear water-white reaction mixtures from which crystalline solids were isolated. These were identified by means of X-ray analysis as unreacted phenylarsonic acid according to the cell constants measured. NMR spectra indicated the presence of various reaction products. These findings suggest that arsenic *may* form compounds with 1,3-diols in a chelating mode but that there seems to be a preference for vicinal diols.

Carbohydrate Chelation. With these results at hand carbohydrates as chelating molecules in *spiro*-arsoranes were introduced. The condensation of phenylarsonic acid and methyl β-D-ribofuranoside (Me-β-D-Rib*f*) yielded sirupy reaction products whose ^{13}C NMR spectra demonstrated the typical pattern of *syn/anti* isomerism in solution. Though all efforts to obtain a crystalline reaction product have not been successful yet, the NMR spectra are interpretable in the sense of a PhAs(Me-β-D-Rib*f*2,3H$_{-2}$)$_2$ with a satisfying degree of confidence stemming from the similarity with the [PhSi(Me-β-D-Rib*f*2,3H$_{-2}$)$_2$]$^-$ analogue.[9] Figure 9c shows the close relationship of the carbohydrate derivative and the respective esters of simple diols.

As often experienced in carbohydrate-(semi)metal chemistry, crystallization used to be hampered in the case of most glycosides. However, there was one exception to the rule: methyl α-D-mannopyranoside (Me-α-D-Man*p*). The condensation product PhAs(Me-α-D-Man*p*2,3H$_{-2}$)$_2$ (**9**) showed the presence of a *spiro* compound where both carbohydrate moieties are bonded to arsenic by their respective *cis*-configured hydroxy groups (Figure 10).

The overall coordination geometry is that of a trigonal bipyramid (3% on the Berry path) with no significant deviations from typical bond lengths and angles. The orientation of the carbohydrate rings in the solid state is found to be *syn/syn*, yet ^{13}C NMR spectra show the presence of all isomers in the solution equilibrium.

NMR Shift Patterns: A Close Spectroscopic Relationship between Silicon and Arsenic. In general, chelation of polyfunctional alcohols, carbohydrates including the nucleosides, and hydroxy carboxylic acids to a central atom is accompanied by a shift of the carbon signals' position in ^{13}C NMR spectra, the "coordination induced shift" (CIS). For pentacoordinate silicon compounds, the CIS values are characterized by values smaller than 10 ppm which are headed both up- and downfield in a typical pattern.[9] An overview of CIS values for **1**−**6** and **9** are given in Table 2. In addition, the *spiro*-arsoranes derived from ethane-1,2-diol, pinacol, benzene-1,2-diol, and naphthalene-2,3-diol were resynthesized according to the literature and included in this table. Furthermore, the *spiro*-arsorane derived from *o*-aminophenol was included. All efforts to obtain ^{13}C NMR

(34) Bibber, J. W.; Barnes, C. L.; Van der Helm, D.; Zuckerman, J. J. *Angew. Chem.* **1983**, *95*, 498–499; *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 501−502.

(35) Gamayurova, V. S.; Kuz'min, V. K.; Chernokal'skii, B. D.; Shagidullin, R. R. *Zhur. Obsh. Khim.* **1973**, *43*, 1937–1939.

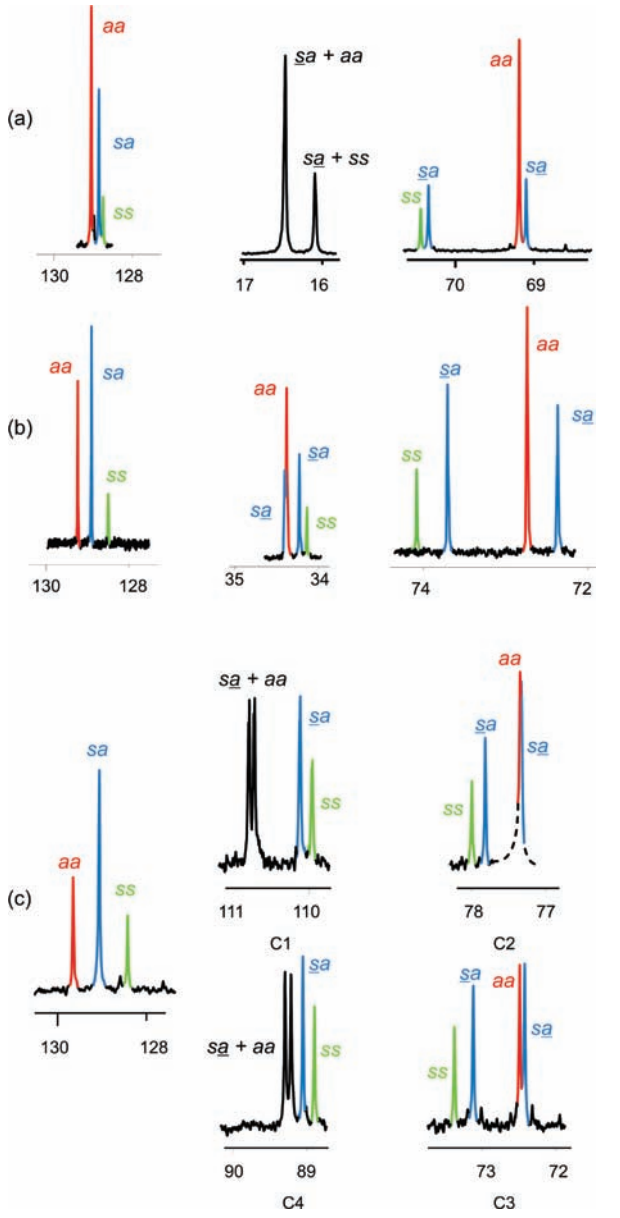


Figure 9. ^{13}C NMR-spectroscopic trace of *syn*/*anti* isomerism. First column, signals of the C_{meta} atoms of the phenyl residue; second column, signals of the carbon atoms adjacent to a As-bonding diol function; third column, signals of the diol carbon atoms. (a) Butane-2,3-diol derivative **1**, (b) *cis*-cyclopentanediol ester **3**, and (c) methyl β-D-ribofuranoside derivative (the atomic numbering refers to the formula in Scheme 2, bottom right). *sa* and *sa* refer to the *syn* and the *anti* part of a *syn*/*anti* pair, respectively.

spectra of **7** and **8** were fruitless because of low solubility in common deuterated solvents.

As can be seen, no coherent picture can be drawn from the obtained values. Thus, no reliable rule seems to exist for either the direction or the absolute values in correlation to the diols' steric pretense or substitution pattern. As a rough trend, the CIS for carbon atoms more distant from the central arsenic atom are found to be greater in absolute values than the carbon atoms bonded to the chelating oxygen atoms except for *meso*-2,3-butanediol and *cis*-1,2-cyclohexanediol. A similar inconclusive picture can be drawn for the CIS values in the ^{1}H NMR spectra which show no correlation to the behavior of the carbon spectra. However, closely related

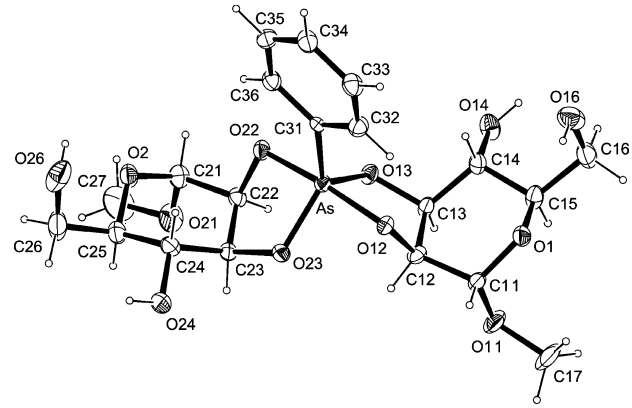


Figure 10. Molecular structure of PhAs(Me-α-D-Man*p*2,3H$_{-2}$)$_2$ in crystals of **9** (50% probability ellipsoids). Distances [Å] and bond angles [deg]: from As to O12 1.829(2), O13 1.785(2), O22 1.818(2), O23 1.781(2), C31 1.905(2); O12−As−O13 88.17(8), O22−As−O23 88.20(8), O12−As−O23 87.26(8), O13−As−O22 86.52(8), O12−As−O22 171.1(1), O13−As−O23 113.26(9); torsion angles [deg]: O12−C12−C13−O13 −42.6(3), O22−C22−C23−O23 −41.0(3); puckering analysis of the chelate rings: As−O12−C12−C13−O13 Q_2 = 0.431(3) Å, φ_2 = 58.0(3)°, twisted on O12−C12, As−O22−C22−C23−O23 Q_2 = 0.431(3) Å, φ_2 = 58.0(3)°, twisted on O22−C22.

Table 2. ^{13}C NMR CIS values for a Series of Phenyl-Substituted *spiro*-Arsoranes[a]

parent acid of chelating molecule	C_α	C_β	C_γ
ethylene glycol	−3.5		
meso-2,3-butanediol	−0.5/−0.4	**−0.5**/−0.8	
	−1.7/−1.8		
pinacol	+2.0	−0.1/−1.0	
cis-1,2-cyclopentandiol	+0.1/−0.3	+3.4/+**3.4**	+1.7/+**1.7**
	−1.2/−1.6	+3.2/+3.1	+1.6
anhydroerythritol	+1.0/+0.8	+2.3/+2.2	
	−0.1	+1.8/+1.7	
exo-cis-2,3-norbornanediol	+1.3/−0.8	**−1.4**/−1.5	≈0.0/−0.5
	−1.9	−1.6	**−0.6**; −0.3
			−0.5
cis-1,2-cyclohexandiol	≈0.0/−0.1	+**0.2**/+0.1	**−0.2**/−0.2
	−1.2/−**1.4**	−0.2/−0.4	−0.3
rac-trans-1,2-cyclohexandiol	+2.0/+1.8	−2.7/−2.8	−0.1/−0.1
	+1.1/+0.7	−3.0/−3.0	−0.1
benzene-1,2-diol	+0.6	−3.9	+0.1
naphthalene-2,3-diol	−0.4	not determined	not determined
methyl α-D-mannopyranoside	**−2.0**/−2.3	+**1.8**/+1.8	not determined
	−2.7/−2.7	+**0.2**/≈ 0.0	
	(anomeric C)	(C2)	
o-aminophenol	+4.0 (C−O);	not determined	not determined
	+2.5 (C−NH)		

[a] CIS values ($\Delta\delta_{diol\ in\ compound} - \Delta\delta_{neat\ diol}$) are given for the carbon atoms adjacent to the arsenic-bonded oxygen/nitrogen atom (C_α) and the subsequent carbon atoms (C_β, C_γ). Multiple numbers indicate appearance of *syn*/*anti* isomers in solution, identical values are due to rounding. CIS values printed in bold face indicate the presence of a predominating isomer according to relative signal intensity.

CIS patterns have been observed for the respective pentacoordinate phenyl silicates, an instructive example being the ribofuranoside spectra (compare Figure 16S in ref 9 and the riboside part of Figure 9 in this work).

Hydrolytic Stability. After having established the close structural and spectroscopic relationship between organylbis(alkylenedioxy)arsoranes and the respective organylbis(diolato)silicates, the hydrolytic behavior of these species was investigated. In previous work, Loiseau et al. have investigated the mechanism of alkaline hydrolysis of *spiro*-arsoranes derived from pinacol as the diol.[24] In this work, hydrolytic stability is claimed for the same compounds under

acidic and neutral conditions. Since earlier reports stated observable hydrolysis in alkaline media or presumed hydrolysis of *spiro*-oxyarsoranes in neutral and acidic aqeous media as well,[18,26] this point was re-evaluated using pinacol as the diol. The respective arsorane was dissolved in deuterated chloroform, and water and aqueous hydrochloric acid (c = 2 mol L^{-1}) was added, respectively, at room temperature. After an induction period of approximately 12 h, ^{13}C NMR spectra were recorded and compared to the spectrum of the compound dissolved in neat deuterated chloroform. In both cases, no signals other than that belonging to the *spiro*-compound were detected thus ruling out cleavage of arsenic−oxygen bonds under the conditions applied. To account for the low miscibility of water and chloroform and to exclude possible doubt whether this might spare the *spiro*-oxyarsorane from hydrolysis, an identical experiment was enacted applying deuterated methanol as solvent. Still, in agreement with Loiseau's work, no cleavage of As−O bonds was detected.

Taking into account the high degree of hydrolytic stability/inertness at neutral and acidic pH values, it appears to be promising to try the synthesis of a *spiro*-arsorane directly from the aqueous solution equilibrium. To do so a stochiometric mixture of phenylarsonic acid and pinacol was suspended in water and brought to incipient boiling slowly evaporating the solvent. The procedure was halted right before all water was driven off from the reaction vessel to prevent the initiation of condensation reactions with molten pinacol. A ^{13}C NMR spectrum of the colorless extract was taken in deuterated chloroform and showed only resonances attributable to the *spiro*-compound which accordingly had formed from the aqueous medium.

Extending the standard procedure, heating of the reaction mixture is not necessary in the presence of water. In addition, the pH value for arsorane formation does not need to be as low as 2. When phenylarsonic acid, pinacol, and sodium hydroxide in a stochiometric composition of 1:2:0.5 were stirred in water and extracted with chloroform, ^{13}C NMR spectra showed the presence of nearly equal amounts of unreacted pinacol and the corresponding *spiro* compound in the organic phase. The pH value at the beginning of the experiment resembled the pK_{a1} value of phenylarsonic acid of 3.6.[36] A physiological pH value, however, is not suitable for arsorane formation. Repeating the latter experiment in a phosphate buffer at pH 7, both the ^{13}C NMR spectra of the aqueous phase and a chloroform extract showed only the presence of unreacted starting materials.

As a result, a high arsorane yield is most suitably reached by the non-aqueous route. The application of water-removing conditions during the synthesis of *spiro*-oxyarsoranes so frequently stated in the literature, however, appears to be unnecessary.

Conclusion

In the periodic system of the elements, arsenic and silicon are related by a diagonal relationship. Accordingly, the members of isoelectronic series of species of the general formulas $PhE(DiolH_{-2})_2$ (E = Si^-, As) share identical features such as (1) the tendency to adopt a pentacoordinate state in a manner similarly developed (in contrast to phosphorus's pronounced tendency to tetracoordination), (2) the same molecular structures, (3) *syn*/*anti* isomerism following approximately the same rules (the relative instability of the *syn*/*syn* isomer; about the same time scale for isomeric transformations), and (4) analytical tools such as ^{13}C NMR spectra sharing common features. However, there is a marked difference between silicon(IV) and arsenic(V): As−OH functions tend much less to polycondensation than do Si−OH groups. The investigation of hydrolytic equilibria for arsenic-acid derivatives is thus not complicated by the thermodynamic trap of a polycondensate.

A rule that is helpful for the search for chelators in the intriguing case of silicon emerges from a comparison of the typical reactivity patterns of the members of the $PhE(DiolH_{-2})_2$ series: a species hydrolyzes outside the stability range of its respective parent hydroxy compound. Hence diol-derived organylsilicates are stable in about the same alkaline pH range where the tentative parent silicates $RSi(OH)_4^-$ are expected to exist, actually, where their dehydrated forms $RSiO(OH)_2^-$ exist. Accordingly, lowering the pH into the neutral range leads to the decomposition of the diolatosilicates just as the parent silicate anions are protonated to the respective silanetriols which, their pK_a roughly being about 13,[37] represent the stable protonation state at pH 7. Analogously, *spiro*-oxyarsoranes exhibit hydrolytic stability in the same pH region where the equivalent hydroxy compound phenylarsonic acid, $PhAsO(OH)_2$, whose tentative ortho form, $PhAs(OH)_4$, is the parent hydroxy compound of the diol esters, is stable. This is the pH range of about 1 or 2 units below the pK_a of phenylarsonic acid. In fact, it has been demonstrated in this work that the *spiro* esters are not only undecomposed in this strongly acidic regime but form from its components. Applied to silicon, we can predict that higher coordinate silicate anions will not be hydrolytically stable at a neutral pH (unless so strong a chelator is found that much higher complex stabilities result than for the biomolecules investigated so far). Positively stated, the search for silicon-chelating biomolecules should include those that are able to chelate silicon in its pH-7-typical protonation state: the four-coordinate electroneutral Si center as the one in $Si(OH)_4$.

Though this work is intended to concentrate on the silicon-mimicking properties of arsenic, it should be noted that the arsenic-biomolecule interaction is a field of lively research itself. In addition to the more covalently bonded As−S and As−C compounds, the latter including C-bonded carbohydrate, mostly 5′-ribofuranosyl-derivatives,[38,39] O-chelating carbohydrate-arsenic compounds may prove significant.

(36) Jaafar, J.; Irwan, Z.; Ahamad, R.; Terabe, S.; Ikegami, T.; Tanaka, N. *J. Sep. Sci.* **2007**, *30*, 391–398.

(37) Kreshkov, A: P.; Andronov, V. F.; Drozdov, V. A. *Russ. J. Phys. Chem.* **1972**, *46*, 1605–1606.

(38) Raab, A.; Wright, S. H.; Jaspars, M.; Meharg, A. A.; Feldmann, J. *Angew. Chem.* **2007**, *119*, 2648–2651; *Angew. Chem. Int. Ed.* **2007**, *46*, 2594−2597.

(39) Mancini, I.; Guella, G.; Frostin, M.; Hnawia, E.; Laurent, D.; Debitus, C.; Pietra, F. *Chem.−Eur. J.* **2006**, *12*, 8989–8994.

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Supporting Information Available: Experimental procedures, ^{1}H- and ^{13}C NMR spectra, melting points, UV/vis spectra, mass spectra, IR and Raman spectra for compounds **2**−**9** and experimental procedures. ^{1}H- and ^{13}C NMR spectra, UV/vis spectra, mass spectra, IR and Raman spectra for the resynthesized compounds from the literature, and information about crystal structure determination. ^{13}C NMR spectra for compounds **1**−**5**, **9**, and PhAs(Me-β-D-Rib*f*2,3H$_{-2}$)$_2$ (graphics) are included to allow for the estimation of *syn*/*anti* ratios. This material is available free of charge via the Internet at http://pubs.acs.org.

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