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## Do Spiroarsoranes Exhibit Polytopal Equilibrium in Solution?

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Received September 1, 2009

The spiroarsoranes 5-phenyl-1,6-dioxo-4,9-diaza-5 $\lambda^5$ -arsaspiro[4.4]nonane (**6**), (3*R*,8*R*)-3,8-dimethyl-5-phenyl-1,6-dioxo-4,9-diaza-5 $\lambda^5$ -arsaspiro[4.4]nonane (**7**), (2*S*,7*S*)-2,7-dimethyl-5-phenyl-1,6-dioxo-4,9-diaza-5 $\lambda^5$ -arsaspiro[4.4]nonane (**8**), and (3*S*,8*S*)-3,8-dimethyl-(2*R*,7*R*)-2,5,7-triphenyl-1,6-dioxo-4,9-diaza-5 $\lambda^5$ -arsaspiro[4.4]nonane (**9**) were prepared by reaction of phenylarsonic acid and the corresponding amino alcohol. The presence of polytopal  $\Delta \rightleftharpoons \Lambda$  equilibrium in **6–9** was demonstrated by HPLC and NMR studies. NBO computations at the MP2/6-31+G(2d,2p) level indicate that methyl substitution in C2 or C3 of the oxazarsolane ring determines the predominance of  $\Delta$  or  $\Lambda$  stereoisomers. GIAO B3LYP/6-311++G(2d,2p) computations were used to assign experimental <sup>1</sup>H and <sup>13</sup>C NMR spectra.

### Introduction

Polytopal equilibrium is the principal structural behavior that any atom in a pentacoordinated state could exhibit.<sup>1</sup> The pentacoordinated state in phosphorus has been studied more thoroughly than for any other elements.<sup>2</sup> Most of the experimental and theoretical studies support the stereochemical nonrigidity of non transition elements; furthermore, fluxional equilibrium in phosphoranes is considered as the principal model for understanding their pentacoordination phenomena. In general, fluxional rates of phosphoranes coincide with the NMR time scale and their exchange processes are easily studied by variable-temperature experiments.<sup>3</sup> However, due

to the great avidity of phosphorus for oxygen, fluxional studies of phosphoranes have been made only in solvents lacking oxygen atoms. Despite the biological relevance of phosphoranes and the consequences of polytopal equilibrium in the stereochemistry of tri- and tetracoordinated phosphorous compounds<sup>4</sup> and, consequently, in their biological activity, it is not possible to make dynamic studies of phosphoranes in water. Arsoranes, on the other hand, are thermodynamically stable compounds in the presence of water and it is not likely that they undergo intermolecular exchange. Accordingly, it would be interesting to study arsorane chemistry in water. Additionally, arsenic and phosphorus have structural and chemical similarities;<sup>5</sup> arsoranes have the ability to mimic phosphorane and interfere in different metabolic processes and, in general, arsenic compounds are toxic.<sup>6</sup> Surprisingly, very little is known about arsoranes. It is known that arsenic centers carry out faster Berry pseudorotation than does phosphorus.<sup>7</sup> However, an additional

<sup>\*</sup>To whom correspondence should be addressed. E-mail: tromero@uaeh.edu.mx.

(1) Holmes, R. R. *Pentacoordinated Phosphorus-Structures and Spectroscopy*; American Chemical Society: Washington, DC, 1980; Vols. I and II, ACS Monographs 175 and 176.

(2) (a) Adachi, T.; Matsukawa, S.; Nakamoto, M.; Kajiyama, K.; Kojima, S.; Yamamoto, Y.; Akiba, K.; Re, S.; Nagase, S. *Inorg. Chem.* **2006**, *45*, 7269–7277. (b) Rzepa, H. S.; Cass, M. E. *Inorg. Chem.* **2006**, *45*, 3958–3963. (c) Hanes, R. E.; Lynch, V. M.; Dalby, K. N. *Org. Lett.* **2002**, *2*, 201–203. (d) Kubo, K.; Nakazawa, H.; Mizuta, T.; Miyoshi, K. *Organometallics* **1998**, *17*, 3522–3531.

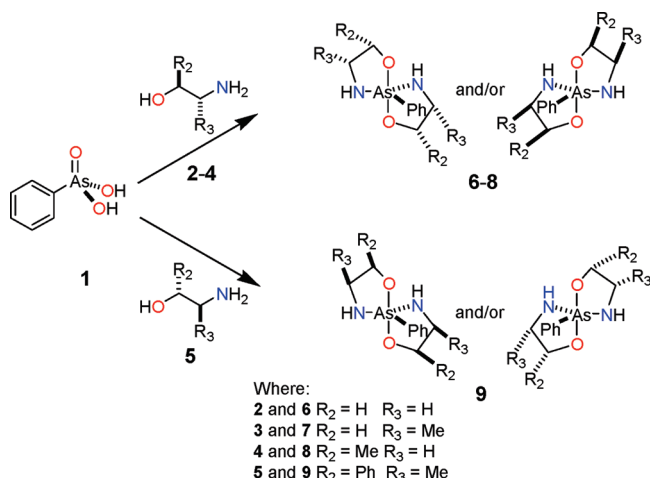
(3) (a) Villaume, S.; Strich, A.; Perera, S. A.; Bartlett, R. J. *J. Phys. Chem. A* **2007**, *111*, 2220–2228. (b) Keijzer, A. E. H.; Koole, L. H.; Buck, H. M. *J. Am. Chem. Soc.* **1988**, *110*, 5995–6001. (c) Clark, T. E.; Day, R. O.; Holmes, R. R. *Inorg. Chem.* **1979**, *18*, 1660–1667. (d) Holmes, R. R.; Deiters, J. A. *J. Am. Chem. Soc.* **1977**, *88*, 3318–3326.

(4) (a) Kumara-Swamy, K. C.; Satish-Kumar, N. *Acc. Chem. Res.* **2006**, *39*, 324–333. (b) Timosheva, N. V.; Chandrasekaran, A.; Holmes, R. R. *Inorg. Chem.* **2006**, *45*, 3113–3123. (c) Holmes, R. R. *Acc. Chem. Res.* **2004**, *37*, 746–753. (d) Gerrata, B.; Sowa, G. A.; Cleland, W. W. *J. Am. Chem. Soc.* **2000**, *122*, 12615–12621. (e) Rauk, A.; Allen, L. C.; Mislow, K. *J. Am. Chem. Soc.* **1972**, *94*, 3035–3040.

(5) (a) Konu, J.; Balakrishna, M. S.; Chivers, T.; Swaddle, T. W. *Inorg. Chem.* **2007**, *46*, 2627–2636. (b) Moc, J.; Morokuma, K. *J. Am. Chem. Soc.* **1995**, *117*, 11790–11797. (c) Moc, J.; Morokuma, K. *Inorg. Chem.* **1994**, *33*, 551–560. (d) Breidung, J.; Thiel, W.; Komomicki, A. *Inorg. Chem.* **1991**, *30*, 1067–1073. (6) (a) Laparra, J. M.; Vélez, D.; Barberá, R.; Montoro, R.; Farré, R. *J. Agric. Food Chem.* **2007**, *55*, 5892–5897. (b) Aposhian, H. V.; Aposhian, M. M. *Chem. Res. Toxicol.* **2006**, *19*, 1–15. (c) Naranmandura, H.; Suzuki, N.; Iwata, K.; Hirano, S.; Suzuki, K. T. *Chem. Res. Toxicol.* **2007**, *20*, 616–624. (d) Zakharyan, R. A.; Tsapraill, G.; Chowdhury, U. K.; Hernandez, A.; Aposhian, H. V. *Chem. Res. Toxicol.* **2005**, *18*, 1287–1295. (e) Radabaugh, T. R.; Sampayo-Reyes, A.; Zakharyan, R. A.; Aposhian, H. V. *Chem. Res. Toxicol.* **2002**, *15*, 692–698.

(7) (a) Jiang, X.; Matsukawa, S.; Yamamichi, H.; Yamamoto, Y. *Inorg. Chem.* **2007**, *46*, 5480–5482. (b) Said, M. A.; Kumara-Swamy, K. C.; Veith, M.; Huch, V. *Inorg. Chem.* **1996**, *35*, 6627–6630. (c) Trinquier, G.; Daudey, J.; Caruana, G.; Madaule, Y. *J. Am. Chem. Soc.* **1984**, *106*, 4794–4799. (d) Bohra, R.; Roesky, H. W. *Adv. Inorg. Radiochem.* **1984**, *28*, 203–254.

**Scheme 1.** Synthesis of Spiroarsoranes **6–9** from Phenylarsonic Acid **1** and 2 Equiv of the Corresponding Amino Alcohols **2–5**<sup>11</sup>



tool in learning the dynamic behavior of phosphoranes that is not available for arsoranes is  $^{31}\text{P}$  NMR (or  $^{19}\text{F}$  NMR when it is connected by one to three bonds to P), where more than one isomer can be readily identified.<sup>8</sup> Thus, it has not yet been determined if arsoranes show polytopal equilibrium in aqueous media. Pentacoordinate compounds prefer to adopt a trigonal-bipyramidal (TBP) geometry.<sup>9</sup> The presence of ring systems imposes constraints that limit their stereochemical possibilities. Thus, five-membered bicyclic compounds assume conformations where ring substituents span axial-equatorial positions and the spiro compounds formed can be optically active.<sup>10</sup> In view of this lack of knowledge about the fluxional behavior of arsoranes in aqueous media, we set out to determine the presence of polytopal equilibria in spiroarsoranes using a set of alcohol amines as bidentate ligands (Scheme 1).

We chose compounds **6–9** because alcohol amines are effective ligands for the slow isomerization of spiroarsoranes. Moreover, we used chiral ethanol amines because they would produce diastereoisomeric spiroarsoranes after exchange processes and, in theory, these molecules must have different physical and chemical properties. In this context, we used NMR spectroscopy and HPLC as tools to study the dynamic behavior of spiroarsoranes **6–9**. Additionally, the crystal structure of **9Δ** gave us experimental data to assess quantum chemical procedures used in the study of ground states of **6–9**. The presence of stereoisomers in spiroarsoranes was corroborated by theoretical NMR studies.

## Experimental Section

All reactions were carried out with magnetic stirring under a nitrogen atmosphere in oven-dried glassware. Alcohol

amines were purchased from commercial suppliers and used without further purification. Phenylarsonic acid was synthesized according to ref 12. Toluene was dried and distilled prior to use.  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a JEOL GX-400 MHz spectrometer. Chemical shifts ( $\delta$ , ppm) are relative to tetramethylsilane (TMS), with the resonances of deuterated and partially deuterated solvents used as internal standards:  $\text{C}_6\text{H}_5$  ( $\delta$  7.16 for proton NMR) and  $\text{C}_6\text{D}_6$  ( $\delta$  128.0 for carbon NMR) or  $\text{CH}_3\text{OH}$  ( $\delta$  3.31 for proton NMR and  $\delta$  49.1 for carbon NMR) as internal reference when  $\text{D}_2\text{O}$  was used. Mass spectra were measured on a JEOL MStation JMS-700 instrument with FAB ionization. High-performance liquid chromatography (HPLC) was performed on an Agilent 1100 Series HPLC system equipped with a Refractive Index detector using an Ultron ES-OVM (chiral) column or an Eclipse XDB-C8 (nonchiral) column. Melting points were measured on a Mel-Temp II apparatus and are uncorrected. The IR spectra were recorded on a Perkin-Elmer System 200 FT-IR spectrophotometer. Elemental analyses were determined on a Perkin-Elmer Series II CHNS/O analyzer 2400 instrument. X-ray diffraction was performed on a Bruker APEX CCD diffractometer.

## Computational Details

All calculations were carried out using Gaussian 98<sup>13</sup> and Q-Chem 3.0.<sup>14</sup> The optimization method was calibrated using experimental data for compound **9** with methyl and phenyl substituents in endo positions (see the Supporting Information). The B3LYP/6-311++G(2d,2p) level was used to optimize structures **6–9**. Reported energy values are ZPE corrected. Harmonic vibrational frequencies were calculated for each optimized structure; in all cases no imaginary frequency was found. NBO analyses were performed at the MP2/6-31+G(2d,2p) level by the NBO 3.1 program included in GAUSSIAN package programs.<sup>15</sup> NMR chemical shift calculations were obtained with the GIAO method at the B3LYP/6-311++G(2d,2p) level.

## Results and Discussion

**NMR and HPLC Studies.** NMR spectra show that the geometry of arsoranes **6–9** in solution is in agreement

(12) Doak, G. O. *J. Am. Chem. Soc.* **1940**, 62, 167–168.

(13) 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.; Stain, 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.; Salvador, P.; Dannenberg, J. J.; 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.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Gead-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98, revision A.11*; Gaussian Inc., Pittsburgh, PA, 2001.

(14) Shao, Y.; Fusti-Molnar, L.; Jung, Y.; Kussmann, J.; Ochsenfeld, C.; Brown, S. T.; Gilbert, A. T. B.; Slipchenko, L. V.; Levchenko, S. V.; O'Neill, D. P.; Distasio, Jr. R. A.; Lochan, R. C.; Wang, T.; Beran, G. J. O.; Besley, N. A.; Herbert, J. M.; Lin, C. Y.; Van Voorhis, T.; Chien, S. H.; Sodt, A.; Steele, R. P.; Rassolov, V. A.; Maslen, P. E.; Korambath, P. P.; Adamson, R. D.; Austin, B.; Baker, J.; Byrd, E. F. C.; Daschel, H.; Doerksen, R. J.; Dreuw, A.; Dunietz, B. D.; Dutoi, A. D.; Furlani, T. R.; Gwaktney, S. R.; Heyden, A.; Hirata, S.; Hus, C.; Kedziora, G.; Khalliulin, R. Z.; Klunzinger, P.; Lee, A. M.; Lee, M. S.; Liang, W.; Ritchie, J.; Rosta, E.; Sherrill, C. D.; Simmonett, A. C.; Subotnik, J. E.; Woodcock III, H. L.; Zhang, W.; Bell, A. T.; Chakraborty, A. K.; Chipman, D. M.; Keil, F. J.; Warshel, A.; Hehre, W. J.; Schaefer III, H. F.; Kong, J.; Krylov, A. I.; Gill, P. M. W.; Head-Gordon, M. *Phys. Chem. Chem. Phys.*, in press.

(15) Glendenning, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F. *NBO (Version 3.1)*; Gaussian Inc., Pittsburgh, PA, 2003.

(8) (a) Jiang, X.; Matsukawa, S.; Yamamoto, Y. *Dalton Trans.* **2008**, 3678–3687. (b) Kojima, S.; Nakamoto, M.; Akiba, K. *Eur. J. Org. Chem.* **2008**, 1715–1722. (c) Kommana, P.; Satish-Kumar, N.; Vittal, J. J.; Jayasree, E. G.; Jemmis, E. D.; Kumara-Swamy, K. C. *Org. Lett.* **2004**, 6, 145–148. (d) Satish-Kumar, N.; Kommana, P.; Vittal, J. J.; Kumara-Swamy, K. C. *J. Org. Chem.* **2002**, 67, 6653–6658. (e) Kumaraswamy, S.; Kommana, P.; Satish-Kumar, N.; Kumara-Swamy, K. C. *Chem. Commun.* **2002**, 40–41.

(9) Gillespie, R. J.; Popelier, P. L. A. *Chemical Bonding and Molecular Geometry-From Lewis to Electron Densities*; Oxford University Press: New York, 2001; Topics in Inorganic Chemistry, p 84.

(10) (a) Mislow, K. *Acc. Chem. Res.* **1970**, 3, 321–331. (b) Dale, A. J.; Froyen, P. *Acta Chem. Scand.* **1975**, B29, 741–748.

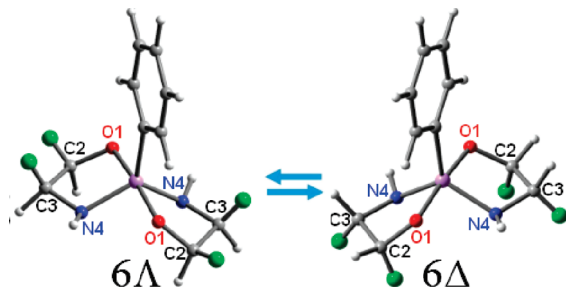
(11) See the Supporting information for the preparation procedure of the spiroarsoranes **6–9**.

**Table 1.**  $^1\text{H}$  NMR (ppm) of Spiroarsoranes **6–8** in  $\text{D}_2\text{O}$ 

	H–C2	H–C3	$\text{CH}_3$	aryl H <sub>ortho</sub>
<b>6</b>	3.75	3.05		7.69
<b>7</b>	3.51 and 3.71	3.36	1.20	7.74
<b>8</b>	3.97	2.79 and 2.98	1.18	7.74

**Table 2.**  $^{13}\text{C}$  NMR (ppm) of Spiroarsoranes **6–8** in  $\text{D}_2\text{O}$ 

	C2	C3	$\text{CH}_3$	$\text{C}_{\text{ipso}}$	$\text{C}_{\text{ortho}}$	$\text{C}_{\text{meta}}$	$\text{C}_{\text{para}}$
<b>6</b>	58.2	41.5		137.4	131.8	129.2	130.0
<b>7</b>	63.5	49.2	14.9	138.2	130.2	129.2	131.7
<b>8</b>	64.6	45.9	19.8	138.2	130.0	129.1	131.6

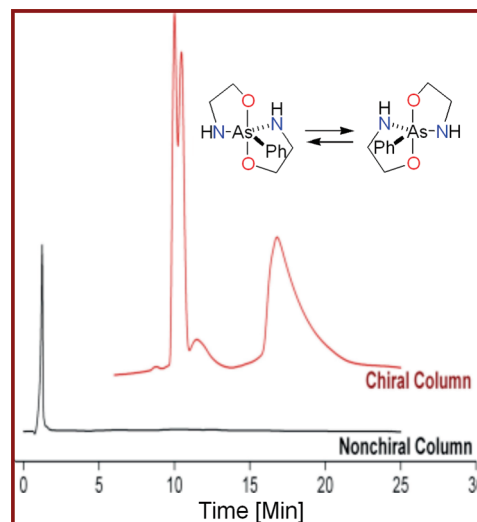
**Scheme 2.** Polytopal Equilibrium  $\Delta \rightleftharpoons \Lambda$  for **6**<sup>a</sup>

<sup>a</sup> In **6 $\Delta$** , hydrogen atoms in green are in exo positions, and in **6 $\Lambda$** , the same hydrogen atoms are in endo positions.

with the VSEPR model of Gillespie (Tables 1 and 2).<sup>9</sup> Compounds **6–9** are dissymmetric ( $C_2$ ) spiroarsoranes with trigonal-bipyramidal geometries where oxygen atoms are in apical positions and the presence of  $\Delta$  and  $\Lambda$  stereoisomers is feasible (Scheme 2).<sup>16</sup> In  $\Delta$  and  $\Lambda$  stereoisomers, the hydrogen atoms of each methylene group have a diastereotopic relation with endo and exo orientations; therefore, they must have different chemical environments. Nevertheless, the  $^1\text{H}$  NMR spectrum of **6** in aqueous solution shows that endo and exo methylene hydrogen atoms have the same chemical shifts (Table 1).

Since the synthesis of spiroarsorane **6** was not stereoselective, the presence of a racemic mixture (**6 $\Delta$**  and **6 $\Lambda$** ) is feasible. However, HPLC studies show that in aqueous solution **6** is not a simple mixture of two enantiomers. When compound **6** is eluted through a nonchiral column, only one signal is detected (Figure 1). In contrast, the use of a chiral column evidences the presence of several stereoisomers of **6**. It is not possible to isolate each stereoisomer eluted from the chiral column, because when they leave the column, they immediately racemize. The NMR and HPLC behavior indicates that **6** presents a dynamic equilibrium when it is in aqueous solution.

It is well known that phosphorus inversion in phosphoranes occurs via a polytopal mechanism that produces a series of intermediate structures of higher energy.<sup>3a,17</sup> Hence, we propose that the inversion of arsenic in spiroarsorane **6** takes place by a similar mechanism. Epimerization is effected through Berry's pseudorotation and, in the case of

**Figure 1.** HPLC chromatograms of spiroarsorane **6**: (black line) elution profile using an Eclipse XDB-C8 (nonchiral) column; (red line) elution profile using an Ultron ES-OVM (chiral) column.

spiroarsorane **6**, the polytopal equilibrium  $\Delta \rightleftharpoons \Lambda$  could have up to eight intermediates with trigonal-bipyramidal geometries (Scheme 3).<sup>18</sup> In Scheme 3,  $\Delta$  and  $\Lambda$  stereoisomers with  $C_2$  symmetry are structures of lower energy and, therefore, they are the predominant chemical species in  $\Delta \rightleftharpoons \Lambda$  equilibrium. According to Bent's rule, more electronegative substituents prefer to occupy the apical site in molecules with TBP geometries. However, during the past decade, different research groups have obtained numerous examples of phosphoranes and arsoranes with reversed apicophilicity.<sup>19</sup> Thus, the presence of TBP intermediates with phenyl and/or N atoms in apical positions is very likely to occur in the inversion of arsenic by pseudorotation. Additional support for Scheme 3 was introduced by Betz and Klüfers, who utilized diol derivatives of phenylarsonic acid.<sup>20</sup> When *meso*-2,3-butanediol was used, three spiroarsoranes were produced, two of them having  $C_2$  symmetry and methyl substituents in endo/endo and exo/exo positions relative to the phenyl group. The third spiroarsorane has  $C_s$  symmetry and methyl substituents in endo/exo positions. In our case,  $\Delta$  and  $\Lambda$  stereoisomers of compounds **7–9** have substituents in endo/endo or exo/exo positions. However, for these compounds any stereoisomer with exo/endo substituents gives a structure of higher energy due to N(apical)–O(apical) disposition.

Although  $\Delta$  and  $\Lambda$  for spiroarsoranes **7** and **8** must be diastereoisomers, their NMR spectra in  $\text{D}_2\text{O}$  show only one set of signals (unfortunately, compound **9** is not

(18) DeBruin, K. E.; Naumann, K.; Zon, G.; Mislow, K. *J. Am. Chem. Soc.* **1969**, *91*, 7031–7040.

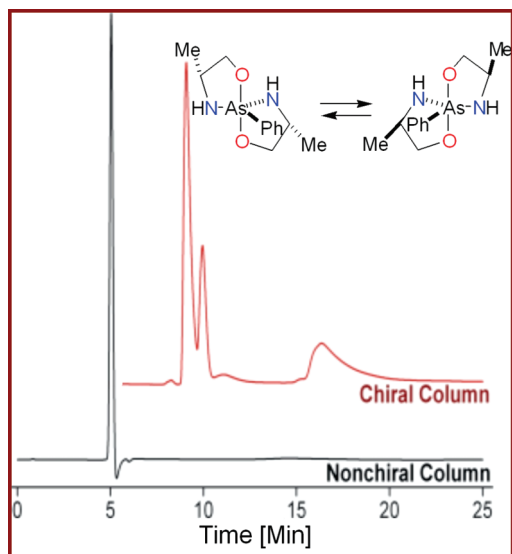
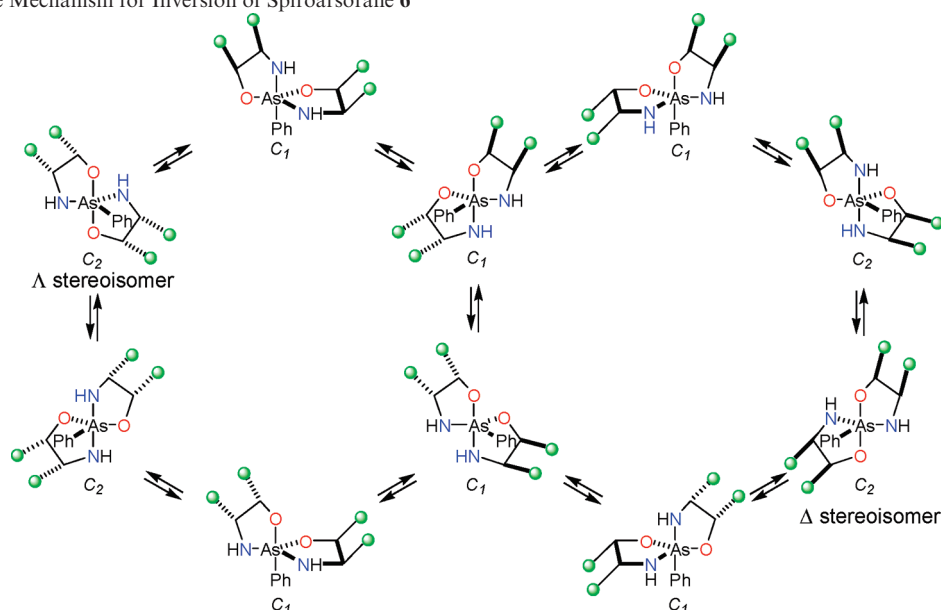
(19) For other examples with “reversed apicophilicity”, see: (a) Kommana, P.; Kumaraswamy, S.; Vittal, J. J.; Kumara-Swamy, K. *C. Inorg. Chem.* **2002**, *41*, 2356–2363. (b) Kajiyama, K.; Yoshimune, M.; Nakamoto, M.; Matsukawa, S.; Kojima, S.; Akiba, K. *Org. Lett.* **2001**, *3*, 1873–1875. (c) Satish-Kumar, N.; Praveen-Kumar, K.; Pavan-Kumar, K. V. P.; Kommana, P.; Vittal, J. J.; Kumara-Swamy, K. *C. J. Org. Chem.* **2004**, *69*, 1880–1889. (d) Kumara-Swamy, K. C.; Praveen-Kumar, K.; Bhuvan-Kumar, N. N. *J. Org. Chem.* **2006**, *71*, 1002–1008. (e) Matsukawa, S.; Kojima, S.; Kajiyama, K.; Yamamoto, Y.; Akiba, K.; Re, S.; Nagase, S. *J. Am. Chem. Soc.* **2002**, *124*, 13154–13170. (f) Kumara-Swamy, K. C.; Balaraman, E.; Phani-Pavan, M.; Bhuvan-Kumar, N. N.; Praveen-Kumar, K.; Satish-Kumar, N. *J. Chem. Sci.* **2006**, *118*, 495–501.

(20) Betz, R.; Klüfers, P. *Inorg. Chem.* **2009**, *48*, 925–935.

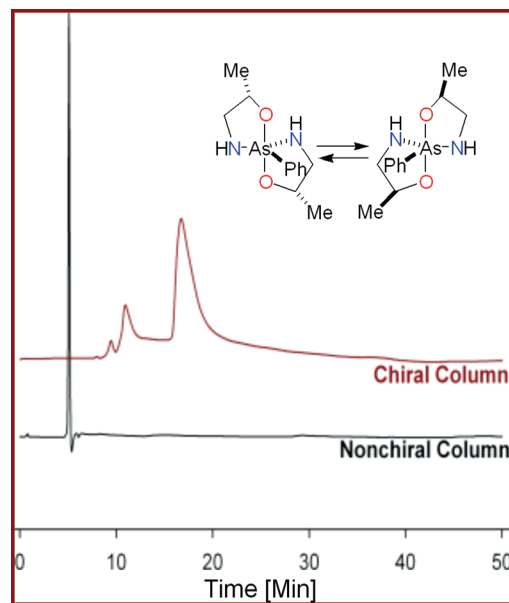
(16) Spiroarsoranes **6–9** are dissymmetric molecules ( $C_2$ ), and therefore we use the  $C_2$  axis as the reference for the  $\Delta$  and  $\Lambda$  designation. See: Liehr, A. D. *J. Phys. Chem.* **1964**, *68*, 3629–3733.

(17) (a) Strich, A.; Veillard, A. *J. Am. Chem. Soc.* **1973**, *95*, 5574–5581. (b) Muetterties, E. L. *J. Am. Chem. Soc.* **1969**, *91*, 4115–4122. (c) Ugi, I.; Marquarding, D.; Klusacek, H.; Gillespie, P.; Ramirez, F. *Acc. Chem. Res.* **1971**, *4*, 288–296.



**Scheme 3.** Probable Mechanism for Inversion of Spiroarsorane **6****Figure 2.** HPLC chromatograms of spiroarsorane **7**: (black) using an Eclipse XDB-C8 nonchiral column; (red) using an Ultron ES-OVM chiral column.

soluble in water and it was not possible to obtain its NMR spectrum in  $D_2O$  solution).<sup>21</sup> Furthermore, HPLC studies using a chiral column reveal, once more, the presence of several stereoisomers of **7** and **8** (Figures 2 and 3). When a nonchiral column was used, only one signal was detected in both cases. Thus, if the  $\Delta \rightleftharpoons \Delta$  polytopal equilibrium exists, it must be very fast. If interconversion between  $\Delta$  and  $\Delta$  is faster than the NMR time scale, only one set of signals will appear in the spectra.<sup>22</sup> Thus, the observed chemical shifts and coupling constants in NMR spectra will be an average

**Figure 3.** HPLC chromatograms of spiroarsorane **8**: (black) using an Eclipse XDB-C8 nonchiral column; (red) using an Ultron ES-OVM chiral column.

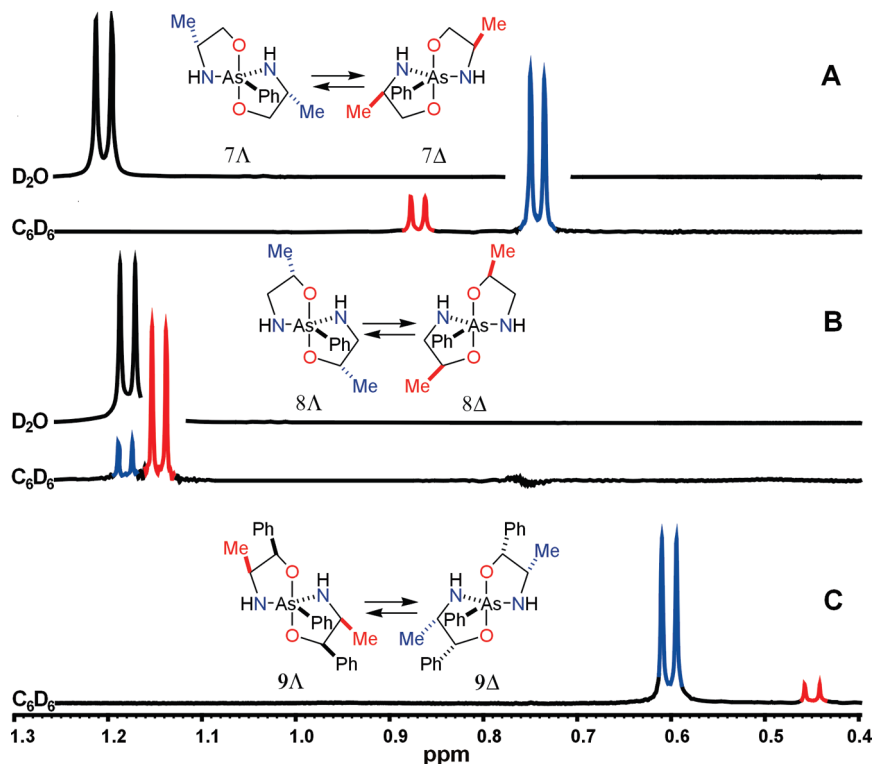
of the  $\Delta$  and  $\Delta$  stereoisomers present and it is not possible to correctly assign hydrogen nuclei in endo and exo positions. On the other hand, the retention time of  $\Delta$  and  $\Delta$  in a nonchiral HPLC column is small, these stereoisomers are preferentially in the mobile phase, and the polytopal equilibrium  $\Delta \rightleftharpoons \Delta$  predominates over the retention equilibrium; therefore, in nonchiral HPLC only one signal is observed.

It is known that a polytopal equilibrium has a dependence on the temperature and the nature of the solvent.<sup>23</sup> Thus, changes in solvent polarity will significantly modify polytopal equilibrium rates. Hence, although spiroarsoranes are not very soluble in solvents of reduced polarity

(21) Spiroarsoranes **6–8** are compounds that are soluble and stable in aqueous media. When the solvent was eliminated from the NMR tubes or samples studied by HPLC, it was possible to recover compounds **6–8**.

(22) Ōki, M. *Applications of Dynamic NMR Spectroscopy to Organic Chemistry*; VCH: Deerfield Beach, FL, 1985; *Methods in Stereochemical Analysis*, Vol. 4, p 2.

(23) Mutttert, E. L. *Tetrahedron* **1974**, *30*, 1595–1604.



**Figure 4.** Methyl signals in  $^1\text{H}$  NMR spectra ( $\text{D}_2\text{O}$  and  $\text{C}_6\text{D}_6$ ) for arsoranes **7** (A), **8** (B), and **9** (C). Methyl groups in endo positions are drawn in blue, and methyl groups in exo positions are drawn in red.

(and compound **6** is totally insoluble),  $^1\text{H}$  NMR spectra of **7–9** were acquired in  $\text{C}_6\text{D}_6$ . In all three cases, two sets of signals, attributed to  $\Delta$  and  $\Lambda$  diastereoisomers, were observed in NMR spectra (Figure 4). As in the case of **6**,  $\Delta$  and  $\Lambda$  stereoisomers of **7–9** have  $C_2$  symmetry and the methyl groups are oriented toward exo and endo positions of the heterocyclic system. When  $\text{CH}_3$  groups occupy exo positions in stereoisomers  $\Delta$  and  $\Lambda$ , they are in the same side than the arsorane phenyl group. However, in endo positions, steric effects and the paramagnetic influence of the arsorane phenyl group on the  $\text{CH}_3$  are minimized. Moreover, it is known that in five-membered heterocycles (such as 1,3,2-oxazaphospholanes) stereoelectronic phenomena determine annular conformation.<sup>24</sup> Thus, it is conceivable that in oxazarsolane rings in  $\Delta \rightleftharpoons \Lambda$  equilibrium anomeric effects decide the predominance of  $\Delta$  or  $\Lambda$  stereoisomers. It is not possible for us to assign with total certainty the experimental  $^1\text{H}$  NMR spectra of **7–9**. However, in compound **8**, having a methyl group next to oxygen, the anomeric effect is likely to play a more decisive role in the annular conformation than in the case of spiroarsoranes **7** and **9**. Therefore, we propose that for compounds **7** and **9** the prevalent species in equilibrium are the stereoisomers with methyl groups in endo positions (**7 $\Delta$**  and **9 $\Delta$**  in Figure 4), and for compound **8** the  $\Delta$  stereoisomer predominates due to methyl groups located in exo positions.

As is observed in Figure 4, the rate of the  $\Delta \rightleftharpoons \Lambda$  polytopal equilibrium in  $\text{C}_6\text{D}_6$  is slower than that in water. Perhaps this rate enhancement is due to polar intermediate structures which are stabilized in water

through hydrogen bonding and allow a faster  $\Delta \rightleftharpoons \Lambda$  polytopal interconversion.

**Crystallographic Studies of 9.** Crystallographic analysis of **9** showed that the unit cell contains only the stereoisomer with methyl and phenyl substituents in endo positions (Figure 5).<sup>25,26</sup> Bond lengths of  $\text{O1–As5}$  (1.855(4) Å),  $\text{As5–N4}$  (1.848(5) Å),  $\text{As5–N4'}$  (1.806(5) Å), and  $\text{As5–C}_{\text{ipso}}$  (1.927(6) Å) are similar to those reported for spiroarsoranes.<sup>7a,27</sup> The length of the  $\text{O1–As5}$  bonds is characteristic of systems with TBP geometry where O atoms are located in apical positions. Structural distortions of TBP geometry were calculated by the dihedral angle method and indicated that As atoms have 57% TBP character.<sup>28</sup> Additionally,

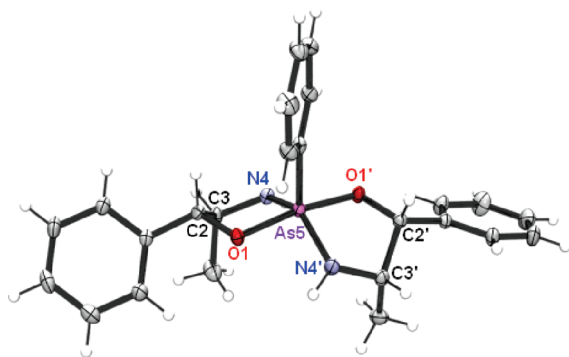
(25) **9 $\Delta$**  was obtained from recrystallization of **9** in benzene/2-propanol. X-ray diffraction studies were performed on a Bruker-APEX diffractometer equipped with a CCD area detector ( $\lambda_{\text{MoK}\alpha}$  = 0.71073 Å, graphite monochromator). Frames were collected at  $T$  = 298 K via  $\omega/\phi$  rotation at 10 s per frame (SMART).<sup>26a</sup> The measured intensities were reduced to  $F^2$  and corrected for absorption with SABADABS (SAINT-NT).<sup>26b</sup> Corrections were made for Lorentz and polarization effects. Structure solution, refinement and data output were carried out with the SHELXTL-NT program package.<sup>26c,d</sup> Crystallographic data for **9 $\Delta$** : monoclinic system, space group  $P2_1$ ,  $a$  = 10.499(2) Å,  $b$  = 5.9685(12) Å,  $c$  = 17.833(4) Å,  $\beta$  = 90.79(3)°,  $V$  = 1117.3(4) Å<sup>3</sup>,  $Z$  = 2, 3838/5272 data/restraints/parameters,  $R1$  ( $I > 2\sigma(I)$ ) = 0.0486,  $wR2$  (all data) = 0.1527, GOF = 1.124.

(26) (a) SMART, Bruker Molecular Analysis Research Tool, Version 5.618; Bruker Analytical X-Ray Systems, Madison, WI, 2000. (b) SAINT+NT Version 6.04; Bruker Analytical X-ray Systems, Madison, WI, 2001. (c) Sheldrick, G. M. SHELX86, Program for Crystal Structure Solution; University of Göttingen, Göttingen, Germany, 1986. (d) SHELXTL-NT Version 6.10; Bruker Analytical X-ray Systems, Madison, WI, 2000.

(27) (a) Goldwhite, H.; Teller, R. G. *J. Am. Chem. Soc.* **1978**, *100*, 5357–5362. (b) Day, R. O.; Holmes, J. M.; Sau, A. C.; Devillers, J. R.; Holmes, R. R.; Deiters, J. A. *J. Am. Chem. Soc.* **1982**, *104*, 2127–2132. (c) Holmes, R. R.; Day, R. O.; Sau, A. C. *Organometallics* **1985**, *4*, 714–720. (d) Poutasse, C. A.; Day, R. O.; Holmes, J. M.; Holmes, R. R. *Organometallics* **1985**, *4*, 708–713.

(28) Muettterties, E. L.; Guggenberger, L. J. *J. Am. Chem. Soc.* **1974**, *96*, 1748–1756.

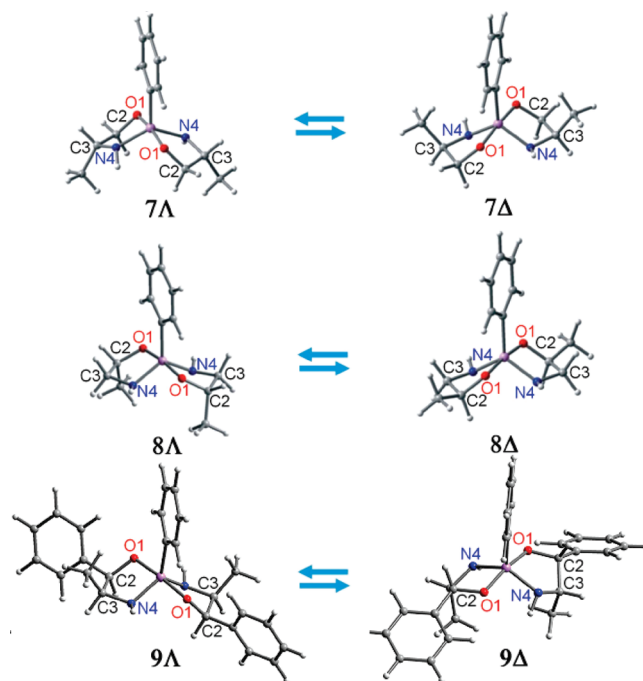
(24) Setzer, W. N.; Black, B. G.; Hovanes, B. A.; Hubbard, J. L. *J. Org. Chem.* **1989**, *54*, 1709–1713.



**Figure 5.** ORTEP drawing of **9Δ** showing thermal ellipsoids at the 20% probability level.

Öki's method shows that N4 and N4' have tetrahedral characters (THC) of 22 and 10%.<sup>29</sup> Also, the N4–C3 (1.457(8) Å) and As5–N4 bond lengths confirm that N atoms do not have trigonal geometries. Moreover, As–N bond lengths in **9Δ** are larger than values reported for compounds with a net As–N double bond and therefore the retrocoordination As=N is not likely to occur in **9Δ**.<sup>30–32</sup>

**Theoretical Studies.** Optimized geometrical parameters (level B3LYP/6-311++G(2d,2p)) of spiroarsorane **9** with methyl and phenyl substituents in endo positions were compared with X-ray experimental results and were found to be similar ( $R^2 = 0.9904$  for lengths and  $R^2 = 0.9955$  for angles). Moreover, the theoretical TBP character for **9Δ** is near (60%) the experimental value (57%). Optimized geometries showed that the presence and orientation of methyl substituents determine the TBP character of spiroarsoranes **7–9**. Thus, an endo orientation of the methyl group on C3 yields spiroarsoranes with 60% TBP character (**7Δ** and **9Δ**). However, when the methyl group on C3 has an exo orientation, the TBP character is nearly 100% (Figure 6). On the other hand, ZPE corrected energies of **6–9** indicated that, in the vapor phase, methyl substitution at C2 or C3 determines the prevalence of Δ or Λ stereoisomers (Table 3). These results are in agreement with the experimental <sup>1</sup>H NMR spectra of **7–9**. It is possible that stereoelectronic effects and steric repulsions are the most important factors that decide the prevalence of a determined stereoisomer. For example, H2 atoms in compounds **8Δ** and **8Λ** have different chemical environments; with H2 endo (**8Δ**) the C2–H2 bond is larger (1.097 Å) than with H2 exo (**8Λ**) (1.094 Å). NBO analysis shows that the O lone pair electrons are more efficiently delocalized toward C2–H<sub>endo</sub> bonds ( $E(n(O) \rightarrow \sigma^*(C2-H_{endo})) = 11.67 \text{ kcal mol}^{-1}$ ) in **8Δ** than toward C2–H<sub>exo</sub> bonds ( $E(n(O) \rightarrow \sigma^*(C2-H_{exo})) = 4.98 \text{ kcal mol}^{-1}$ ) in **8Λ** (Table 4). Thus, better hyperconjugation of C2–H<sub>endo</sub> bonds produces an additional stabilization of **8Δ** and it predominates in the Δ ⇌ Λ equilibrium. On the other hand, methyl substitution



**Figure 6.** B3LYP/6-311++G(2d,2p) optimized geometries of compounds **7–9**.

on C3 produces an inverse phenomenon: that is, nitrogen atoms in spiroarsoranes **6–9** are pyramidal and they do not have any electronic delocalization toward the arsenic atom. The principal consequence of this fact is that nitrogen atoms are able to delocalize their lone pairs toward C3–H bonds. However, for spiroarsoranes **7** hyperconjugation is better toward C3–H<sub>exo</sub> bonds ( $E(n(N) \rightarrow \sigma^*(C3-H_{exo})) = 7.62 \text{ kcal mol}^{-1}$ ) in **7Δ** than toward C3–H<sub>endo</sub> bonds ( $E(n(N) \rightarrow \sigma^*(C3-H_{endo})) = 3.40 \text{ kcal mol}^{-1}$ ) in **7Λ**. Therefore, it is proposed that **7Δ** predominates in the Δ ⇌ Λ equilibrium.

GIAO values and NBO studies of spiroarsoranes **7–9** are in accordance with experimental <sup>1</sup>H NMR spectra ( $R^2 = 0.9858$ – $1.000$  for <sup>1</sup>H NMR). In the ground state, oxazarsolane rings of spiroarsoranes **6–9** have half-chair conformations. In compound **8Δ** a  $n(O) \rightarrow \sigma^*(C2-CH_{3endo})$  stereoelectronic effect occurs (Table 4). The endo methyl groups are axial, and a lone pair (in an anti position) of the vicinal oxygen atom is delocalized toward the C2–CH<sub>3</sub> bond ( $E(n(O) \rightarrow \sigma^*(C2-CH_{3endo})) = 9.77 \text{ kcal mol}^{-1}$ ). Thus, methyl <sup>1</sup>H NMR resonances are shifted toward higher frequencies (Table 5). On the other hand, exo methyl groups in **8Δ** are equatorial and the influence of oxygen is negligible ( $E(n(O) \rightarrow \sigma^*(C2-CH_{3exo})) = 2.31 \text{ kcal mol}^{-1}$ ). Therefore, methyl <sup>1</sup>H NMR resonances of **8Δ** ( $\delta_{\text{experimental}} 1.18$ ,  $\delta_{\text{theoretical}} 1.30$ ) are at higher frequencies than in the case of **8Λ** ( $\delta_{\text{experimental}} 1.15$ ,  $\delta_{\text{theoretical}} 1.23$ ). For **7Δ** and **9Δ** the endo methyl groups are in equatorial positions; however, the stereoelectronic effect of the lone pairs of nitrogen atoms toward the C3–CH<sub>3</sub> bond is different in both compounds. Thus, for **7Δ** the effect of the lone pairs of nitrogen atom is minimal ( $E(n(N) \rightarrow \sigma^*(C3-CH_{3endo})) = 2.14 \text{ kcal mol}^{-1}$ ) and for **9Δ** the lone pairs of nitrogen are delocalized efficiently toward the C3–CH<sub>3</sub> bond ( $E(n(N) \rightarrow \sigma^*(C3-CH_{3endo})) = 8.70 \text{ kcal mol}^{-1}$ ). The opposite

(29) Toyota, A.; Öki, M. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1832–1840.

(30) Matano, Y.; Nomura, H.; Suzuki, H.; Shiro, M.; Nakano, H. *J. Am. Chem. Soc.* **2001**, *123*, 10954–10965.

(31) Krannich, L. K.; Thewalt, U.; Cook, W. J.; Jain, S. R.; Sisler, H. H. *Inorg. Chem.* **1973**, *12*, 2304–2313.

(32) Ahlemann, J. T.; Künzel, A.; Roesky, H. W.; Noltemeyer, M.; Markovskii, L.; Schmidt, H. G. *Inorg. Chem.* **1996**, *35*, 6644–6645.

(33) See the Supporting Information for complete NBO analysis, at the MP2/6-31+G(2d,2p) level, on the hyperconjugation of O–C–H and N–C–H systems for spiroarsoranes **6–9**.

**Table 3.** B3LYP/6-311++G(2d,2p) Electronic Energies (Zero Point Corrected) for Spiroarsoranes 6–9

compd	$E_{\Delta}$ (hartree)	$E_{\Lambda}$ (hartree)	$E_{\Lambda} - E_{\Delta}$ (hartree)	$E_{\Lambda} - E_{\Delta}$ (kcal mol <sup>-1</sup> )
6	-2 885.864 168	-2 885.864 168	0.000 00	0.000
7	-2 964.464 881	-2 964.466 091	-0.001 21	-0.759
8	-2 964.473 243	-2 964.469 509	0.003 73	2.343
9	-3 426.542 262	-3 426.536 740	0.005 52	3.465

**Table 4.** NBO Analysis, Computed at the MP2/6-31+G(2d,2p) Level, for  $\Delta$  and  $\Lambda$  Stereoisomers of Spiroarsoranes 6–9<sup>33</sup>

param	6	7 $\Delta$	7 $\Lambda$	8 $\Delta$	8 $\Lambda$	9 $\Delta$	9 $\Lambda$
Bond Lengths (Å)							
C2–H2 <sub>exo</sub>	1.091	1.097	1.091		1.094	1.102	
C2–H2 <sub>endo</sub>	1.095	1.101	1.100	1.097			1.102
C3–H3 <sub>exo</sub>	1.096		1.095	1.097	1.096	1.096	
C3–H3 <sub>endo</sub>	1.091	1.099		1.092	1.091		1.098
$E$ (kcal mol <sup>-1</sup> )							
n(O)→ $\sigma^*$ <sub>C2–H2<sub>exo</sub></sub>	3.07	2.60	2.04		4.98	10.16	
n(O)→ $\sigma^*$ <sub>C2–H2<sub>endo</sub></sub>	11.34	11.38	12.24	11.67			10.78
n(O)→ $\sigma^*$ <sub>C2–CH3</sub>				2.31	9.77		
n(N)→ $\sigma^*$ <sub>C3–H3<sub>exo</sub></sub>	10.43		7.62	10.62	10.51	3.48	
n(N)→ $\sigma^*$ <sub>C3–H3<sub>endo</sub></sub>	3.22	3.40		3.23	2.98		3.23
n(N)→ $\sigma^*$ <sub>C3–CH3</sub>		9.98	2.14			8.70	9.14

**Table 5.** <sup>1</sup>H NMR (ppm) Calculated with B3LYP/6-311++G(2d,2p)<sup>a</sup> for Spiroarsoranes 6–9

	H <sub>endo</sub> –C2	H <sub>exo</sub> –C2	H <sub>endo</sub> –C3	H <sub>exo</sub> –C3	CH <sub>3</sub>	H <sub>ortho</sub>	$R^{2b}$
6 $\Delta$ and 6 $\Lambda$	4.13	4.14	2.96	3.01		8.88	
7 $\Delta$	4.36	3.87	3.36		0.91	9.07	0.9972
7 $\Lambda$	3.08	3.96		3.13	1.09	8.81	0.9958
8 $\Delta$	4.23		2.99	2.42	1.23	8.95	0.9966
8 $\Lambda$		4.35	2.76	3.11	1.30	8.80	0.9971
9 $\Delta$		5.01		3.55	0.75	8.67	1.0000
9 $\Lambda$	5.61		3.48		0.43	9.09	0.9999

<sup>a</sup> TMS at 31.82 ppm. <sup>b</sup> Calculated on the basis of experimental data obtained in C<sub>6</sub>D<sub>6</sub> without meta and para aromatic hydrogens.

effect is present in spiroarsoranes 7 $\Delta$  and 9 $\Lambda$ . The lone pairs of nitrogen are delocalized efficiently toward the C3–CH<sub>3</sub> bond:  $E(n(N) \rightarrow \sigma^*(C3-CH_{3exo})) = 9.98$  kcal mol<sup>-1</sup> for 7 $\Delta$  and 9.14 kcal mol<sup>-1</sup> for 9 $\Lambda$ . Moreover, methyl <sup>1</sup>H NMR resonances of 7 $\Lambda$  ( $\delta_{\text{experimental}}$  0.74,  $\delta_{\text{theoretical}}$  1.09) and 9 $\Delta$  ( $\delta_{\text{experimental}}$  0.60,  $\delta_{\text{theoretical}}$  0.75) are at higher frequencies than for 7 $\Delta$  ( $\delta_{\text{experimental}}$  0.87,  $\delta_{\text{theoretical}}$  0.91) and 9 $\Lambda$  ( $\delta_{\text{experimental}}$  0.45,  $\delta_{\text{theoretical}}$  0.43). Thus, stereoelectronic effects of lone pairs of oxygen and nitrogen atoms determine the prevalence of  $\Delta$  or  $\Lambda$  stereoisomers and explain their <sup>1</sup>H NMR spectra.

Due to the insolubility of 6 and low solubility of 8 $\Lambda$  spiroarsoranes in C<sub>6</sub>D<sub>6</sub>, it was not possible to obtain their experimental <sup>13</sup>C NMR spectra. However, GIAO calculations indicate that <sup>1</sup>H and <sup>13</sup>C resonances of 7–9 have

**Table 6.** <sup>13</sup>C NMR Chemical Shifts for Spiroarsoranes 6–9 Calculated with B3LYP/6-311++G(2d,2p)<sup>a</sup>

	C2	C3	CH <sub>3</sub>	C <sub>i</sub>	C <sub>o</sub>	C <sub>m</sub>	C <sub>p</sub>	$R^{2b}$
6 $\Delta$ and 6 $\Lambda$	66.6	45.6		151.1	142.3	133.4	136.3	
7 $\Delta$	72.3	54.8	24.6	156.7	142.7	134.5	137.4	0.9934
7 $\Lambda$	73.5	52.3	19.6	148.7	139.6	133.1	135.9	0.9993
8 $\Delta$	73.8	52.6	21.9	151.3	142.2	132.9	135.9	0.9992
8 $\Lambda$	73.1	48.4	24.0	150.6	141.8	133.1	136.0	
9 $\Delta$	80.1	60.5	21.2	149.3	140.2	134.3	137.2	0.9927
9 $\Lambda$	84.3	60.8	20.2	157.6	140.5	134.5	137.5	0.9940

<sup>a</sup> TMS at 183.78 ppm. <sup>b</sup> Calculated on the basis of experimental data obtained in C<sub>6</sub>D<sub>6</sub> without aromatic carbons.

the same behavior ( $R^2 = 0.9927$ – $0.9993$  for <sup>13</sup>C NMR) (Table 6). Stereoelectronic phenomena determine the <sup>13</sup>C resonance frequencies of methyl groups in spiroarsoranes 7 and 8. An efficient delocalization of O or N lone pairs toward the C–CH<sub>3</sub> bond causes electronic deprotection of the methyl carbon, and their resonance frequencies are shifted toward higher values. This phenomenon is corroborated with spiroarsoranes 9: <sup>13</sup>C NMR signals of exo methyl groups in 9 $\Lambda$  ( $\delta_{\text{experimental}}$  18.8,  $\delta_{\text{theoretical}}$  20.2) are at lower frequencies than for endo methyl groups in 9 $\Delta$  ( $\delta_{\text{experimental}}$  19.7,  $\delta_{\text{theoretical}}$  21.2).

## Conclusions

The use of a chiral column in HPLC shows that spiroarsoranes 6–8 present fast polytopal equilibria in aqueous solution. The speed of polytopal equilibria are slower in C<sub>6</sub>D<sub>6</sub> solutions, and the presence of  $\Delta$  and  $\Lambda$  stereoisomers with symmetry C<sub>2</sub> is demonstrated by experimental NMR. Theoretical studies confirm the presence of  $\Delta$  and  $\Lambda$  stereoisomers in compounds 7–9 and suggest that stereoelectronic phenomena determine the prevalence of stereochemical species in  $\Delta \rightleftharpoons \Lambda$  equilibria.

**Acknowledgment.** This work was supported by CONACyT (grant J33279-E). F.P.-G. thanks CONACyT for a scholarship.

**Supporting Information Available:** Text, tables, figures, and CIF files giving experimental procedures, characterization data, NMR spectra, crystallographic information, HPLC chromatograms, absolute energies and zero-point energies, B3LYP optimized structures, and GIAO B3LYP data. This material is available free of charge via the Internet at <http://pubs.acs.org>.