1,4-Dihydro-1,4-diarsinine: Facile Synthesis via Nonvolatile Arsenic Intermediates by Radical Reactions

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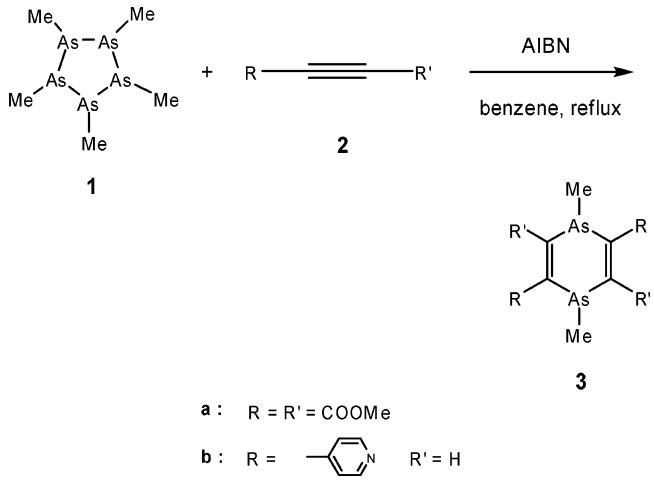
Received January 26, 2007

*Summary: Novel cyclic organodiarsenic compounds, 1,4-dihydro-1,4-diarsinines, were synthesized by radical reactions of pentamethylcyclopentaarsine (**1**) and acetylenic compounds. The radical reactions of **1** and acetylenic compounds such as dimethyl acetylenedicarboxylate (**2a**) and 4-ethynylpyridine (**2b**) in refluxing benzene with 2,2′-azobis(isobutyronitrile) (AIBN; 5 mol %) under a nitrogen atmosphere provided the corresponding 1,4-dihydro-1,4-diarsinines (**3**). Formation of 1,4-dihydro-1,4-diarsinine was confirmed by ^{1}H and ^{13}C NMR spectra and FAB-mass spectrometry. The structures of **3** were confirmed as cis(e,e) forms by X-ray crystallography. This is a facile synthesis of cyclic organodiarsenic compounds, in which no volatile toxic intermediates such as arsenic chlorides and arsenic hydrides were used. Moreover, this is the first example of the synthesis of 1,4-dihydro-1,4-diarsinines.*

Introduction

Organoarsenic compounds have been known since tetramethyldiarsine was prepared in 1760.[1] The discovery of the chemotherapeutic properties of "Salvarsan"[2] led to a rapid expansion of the work of arsenic derivatives. Alkyl- and arylarsines act as ligands for transition metals. Arsines have been reported to be ligands superior to phosphines in a number of transition-metal-catalyzed organic reactions, due to their poorer σ-donor ability.[3] Osmium complexes with arsenic ligands have greater quantum yields and rates of phosphorescence, in which system the heavy-atom effect of the arsenic atom helps to increase spin−orbit coupling.[4] However, most of the organoarsenic compounds used for complexations have been prepared from arsenic chlorides or arsenic hydrides.[5] Ultimate care should be taken in the handling of these arsenic intermediates, due to their volatility. To stimulate the field of organoarsenic chemistry, practical synthetic methods should be discovered.

Scheme 1



Recently, we have reported the synthesis of arsenic-containing polymers, poly(vinylenearsines), by ring collapsed radical alternating copolymerization (RCRAC) of cyclooligoarsines and phenylacetylene or its derivatives.[6] Here, we report the facile synthesis of 1,4-dihydro-1,4-diarsinines (**3**), which were obtained instead of poly(vinylenearsines) by changing the reaction conditions and the acetylenic compounds (Scheme 1). Although *o*-phenylenebis(methylphenylarsine)[7] and related derivatives and cyclic organodiarsenic compounds[8] are already known, this is the first report of the synthesis of 1,4-dihydro-1,4-diarsinines. Advantages of this novel synthetic method of **3** are as follows. First, no volatile toxic intermediates such as arsenic chlorides or arsenic hydrides are used. Cyclooligoarsines are prepared quite easily by reduction of the corresponding arsenic acids or their salts with hypophosphorous acid.[9] Second, the reaction

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10.1021/om070080g CCC: $37.00
Publication on Web 02/24/2007

Table 1. Crystallographic Data for 3a and 3b

	3a	3b
empirical formula	$C_{14}H_{18}O_8As_2$	$C_{16}H_{16}N_2As_2$
formula wt	464.13	386.16
cryst habit	colorless, block	colorless, block
cryst size (mm)	0.50 × 0.40 × 0.30	0.60 × 0.50 × 0.30
cryst syst	orthorhombic	monoclinic
space group	$P2_12_12_1$ (No. 19)	$P2_1/c$ (No. 14)
a (Å)	8.706(10)	10.073(16)
b (Å)	11.434(17)	9.013(2)
c (Å)	18.230(3)	17.420(3)
β (deg)	90	100.626(8)
V (Å^3)	1814.8(5)	1554.5(5)
Z	4	4
D_{calcd} (g cm^{-3})	1.699	1.650
μ (mm^{-1})	3.720	4.292
radiation (Å)	Mo Kα, 0.710 75	Mo Kα, 0.710 75
T (K)	133	123
$2\theta_{max}$	54.9	55.0
no. of rflns collected	16 537	13 778
no. of indep rflns	4052 (R_{int} = 0.072)	3553 (R_{int} = 0.072)
no. of obsd data	3033 ($I > 2\sigma(I)$)	3261 ($I > 2\sigma(I)$)
no. of variables	235	182
residual density (e Å^{-3})	1.22 to −0.45	1.05 to −0.60
R1	0.0376	0.0893
wR2	0.0906	0.0363
GOF	1.008	1.000

proceeds under moderate conditions: i.e., radical reaction in refluxing benzene (at 78 °C). Third, only a common radical initiator is required in addition to the starting compounds. Moreover, this facile reaction provides unique cyclic organodiarsenic compounds. Since the 1,4-dihydro-1,4-diarsinines have two arsenic atoms connected by two rigid bridges, they are considered to be more conformationally restricted than bidentate arsine ligands such as *o*-phenylenebis(dimethylarsine) and 1,2-bis(diphenylarseno)ethylene. The inversion barrier for the trivalent arsine center is high enough to keep the stereochemical structure at room temperature.[10]

Results and Discussion

1,4-Dihydro-1,4-dimethyl-2,3,5,6-tetramethoxycarbonyl-1,4-diarsinine (**3a**) was prepared by the radical reaction of pentamethylcyclopentaarsine (**1**) and dimethyl acetylenedicarboxylate (**2a**). Under a nitrogen atmosphere, a benzene solution of 2,2′-azobis(isobutyronitrile) (AIBN; 5 mol %) was added to a refluxing benzene solution of **2a** and **1**. After the solution was refluxed for 15 h, the solvent was removed to obtain a yellow solid. The obtained solid was dissolved in dichloromethane, and *n*-hexane was added to remove oligomeric products[11] as a yellow precipitate. From the *n*-hexane-soluble part, pure **3a** was isolated by recrystallization from acetonitrile. The yield of isolated **3a** was 34%. Formation of 1,4-dihydro-1,4-diarsinine was confirmed by ^{1}H and ^{13}C NMR and FAB-mass spectrometry. Both the ^{1}H and ^{13}C NMR spectra showed peaks which suggested that **3a** has a vinylenearsine structure. From the FAB-mass spectrometry, **3a** appeared to be a dimer of the vinylenearsine. The stereochemical structure of **3a** in the crystal form was determined by X-ray crystallography. Crystallographic data are given in Table 1. Figure 1 shows that **3a** was the cyclic dimer of the vinylenearsine *cis*(e,e)-1,4-dihydro-1,4-diarsinine. The intramolecular As−As distance is 340 pm, which is shorter than the sum of the van der Waals radii (370 pm).[12] The ring has a boat form, and both of the methyl groups on the arsenic atoms are in equatorial positions. The two lone pairs on the arsenic atoms are directed toward the same side of the ring structure. Because the ORTEP drawing of **3a** showed the divergent syn conformation of the lone pairs, the arsenic donors of **3a** cannot chelate with a transition metal. Therefore, **3a** may form binuclear complexes with different metals.

The radical reaction of **1** and another acetylenic compound with a conjugative substituent, 4-ethynylpyridine (**2b**), also provided the corresponding 1,4-dihydro-1,4-diarsinine. One isomer of **3b** was isolated by recrystallization. As shown by ^{1}H and ^{13}C NMR, FAB-mass spectrometry, and X-ray crystallography, the isolated **3b** also appeared to have the structure of 1,4-dihydro-1,4-diarsinine with C_2 symmetry (Figure 2). The ^{1}H NMR spectrum of **3b** showed a peak for the vinyl proton at δ 6.91 ppm. In the ^{13}C NMR spectrum, single peaks attributed to each of the vinyl carbons appeared at δ 136.9 and 149.7 ppm. The two pyridines are substituted at the para positions of the 1,4-dihydro-1,4-diarsinine. In the case where 2-ethynylpyridine (**2c**) was used, although isolation by recrystallization failed, the presence of the 1,4-dihydro-1,4-diarsinine structure was confirmed by ^{1}H and ^{13}C NMR and FAB-mass spectrometry.[13]

On the basis of the proposed mechanism for RCRAC of **1** and acetylenic compounds previously reported by us,[6] Scheme 2 shows a possible proposed mechanism for this radical reaction. First, AIBN cleaved the As−As bonds of **1** to produce arsenic radicals, followed by the homolytic spontaneous cleavage of the other As−As bonds due to their instability by the destruction of the quite stable five-membered-ring structure. In competition with this reaction, the arsenic radical attacked the ethynyl group of **2** to produce a vinyl radical.[6] Next, a *Z*-form of the vinyl radical converted to an *E*-form of the vinyl radical. Because the unstable As−As bond provides arsenic radicals, the *E*-form of the vinyl radical (*E*-form-a) can be regarded as a biradical form, denoted as *E*-form-b in Scheme 2. Then, the cyclization of *E*-form-b radicals provides **3**. Conversion of the *Z*-form of the vinyl radical to the *E*-form might be a key process in the present reaction, and this process was highly affected by the substituents of the acetylenic compounds and concentrations of the reactants. Under the present conditions, the lifetime of the vinyl radical is long enough to convert from the *Z*-form of the vinyl radical to the thermodynamically favored *E*-form. Reducing the reaction temperature to room temperature gave a trace amount of **3**, probably because of the poorer isomerization of the vinyl radicals.

The ^{1}H NMR spectrum of crude **3a** before recrystallization showed two peaks in the region of methyl protons. A possible isomer of **3a** might be *trans*-**3a**, as shown in Chart 1. Because no pair of peaks with the same area was obtained in the ^{1}H NMR spectrum of crude **3a**, flipping of the ring structure might occur in solution.

(10) Weston, R. E. *J. Am. Chem. Soc.* **1954**, *76*, 2645−2648.

(11) The ^{1}H NMR spectrum of the precipitate showed a broad peak at 6.3−6.1 ppm attributed to the vinyl proton of an oligomeric vinylenearsine structure. The other broad peaks were also assigned to the protons on the oligomeric vinylenearsine compound.

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(13) 1,4-Dihydro-1,4-dimethyl-2,5-bis(2-pyridyl)-1,4-diarsinine (**3c**) was prepared in a fashion similar to that for **3a**, but satisfactory recrystallization failed because of the low crystallinity. Yield of the mixture: 50%. **3c** was a mixture of several isomers. ^{1}H NMR (δ in $CDCl_3$, ppm): 8.7−8.4 (2H, 6-pyr *H*), 7.8−7.5, 7.5−7.35, 7.35−7.2 7.2−7.05 (8H, J = 6 Hz, 3,4,5-pyr *H*, C=C*H*), 1.52, 1.42, 1.3−1.2, 0.87 (6H, AsC*H*$_3$). ^{13}C NMR (δ in $CDCl_3$, ppm, main peak only): 159.1 (2-pyr *C*), 151.8 (pyr *C*=CH), 148.6 (6-pyr *C*), 140.7 (*H*C=C pyr), 136.1 (4-pyr *C*), 121.7 (5-pyr *C*), 119.5 (3-pyr *C*), 9.0 (AsCH_3). HR FAB-MS (*m*/*z*): calcd for [$C_{16}H_{16}N_2As_2^+ - CH_2Cl_2$], 385.9745; obsd, 385.9743; error, −0.2.

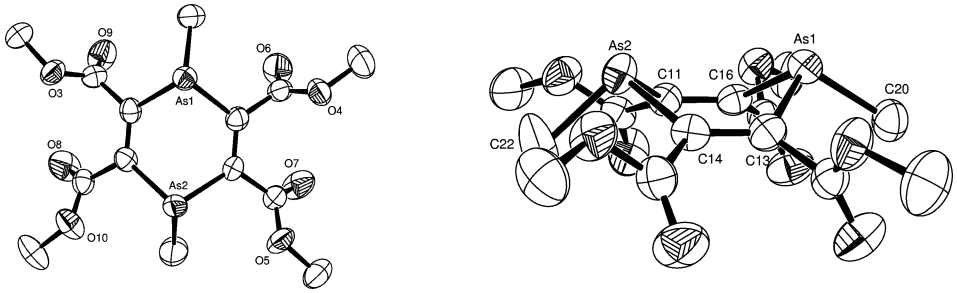


Figure 1. ORTEP drawing of *cis*(e,e)-**3a** isolated by recrystallization from CH_3CN, with thermal ellipsoids shown at the 50% probability level. The hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): As(1)−C(13) = 1.984(5), As(1)−C(16) = 1.973(5), As(1)−C(20) = 1.947(5), As(2)−C(11) = 1.972(5), As(2)−C(14) = 1.964(5), As(2)−C(22) = 1.960(8), C(11)−C(16) = 1.337-(7), C(13)−C(14) = 1.342(7); C(13)−As(1)−C(16) = 94.9(2), C(13)−As(1)−C(20) = 101.2(2), C(16)−As(1)−C(20) = 101.4(2), C(11)−As(2)−C(14) = 96.8(2), C(11)−As(2)−C(22) = 97.0(2), C(14)−As(2)−C(22) = 97.1(2).

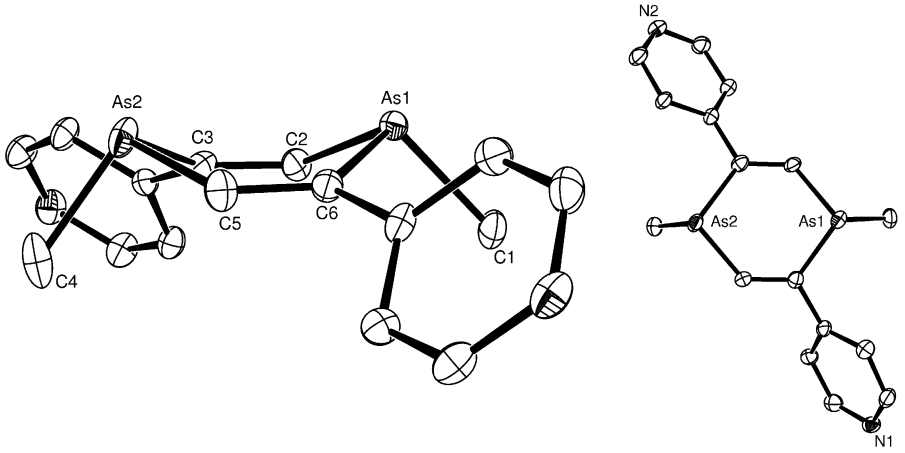
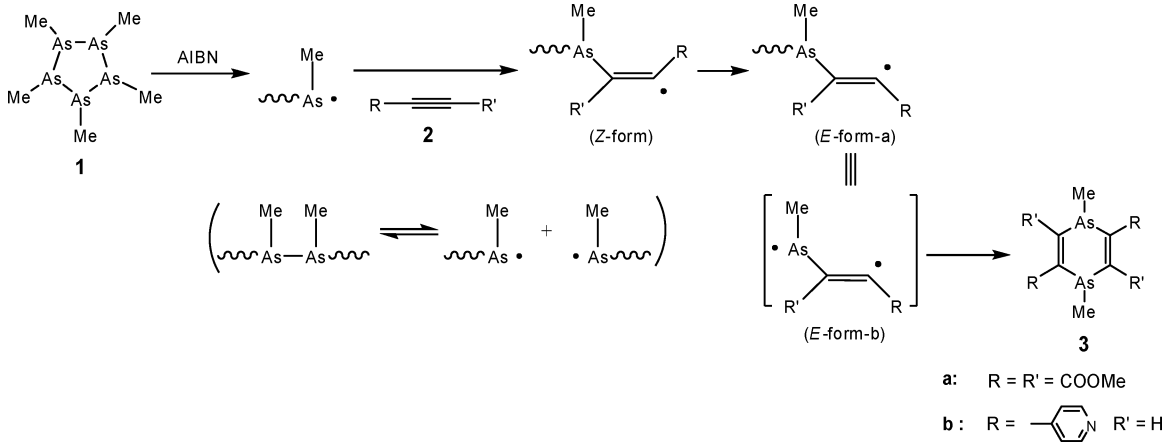


Figure 2. ORTEP drawing of *cis*(e,e)-**3b** isolated by recrystallization from CH_3CN, with thermal ellipsoids shown at the 50% probability level. The hydrogen atoms are omitted for clarity. Selected bond lengths (Å) and angles (deg): As(1)−C(1) = 1.975(3), As(1)−C(2) = 1.938(3), As(1)−C(6) = 1.959(3), As(2)−C(3) = 1.958(3), As(2)−C(4) = 1.973(4), As(2)−C(5) = 1.935(3), C(2)−C(3) = 1.342(4), C(5)−C(6) = 1.336(4); C(1)−As(1)−C(2) = 98.38(15), C(1)−As(1)−C(6) = 100.26(14), C(2)−As(1)−C(6) = 97.31(13), C(3)−As(2)−C(4) = 97.61(15), C(3)−As(2)−C(5) = 98.17(14), C(4)−As(2)−C(5) = 95.75(16).

Scheme 2



Conclusion

We successfully synthesized 1,4-dihydro-1,4-diarsinines (**3**) by the radical reactions of acetylenic compounds and cyclooligoarsine. This is the first synthesis of 1,4-dihydro-1,4-diarsinines, which appeared to have the boat forms with the flagpole positions of the lone pairs on the arsenic atom in the solid state.

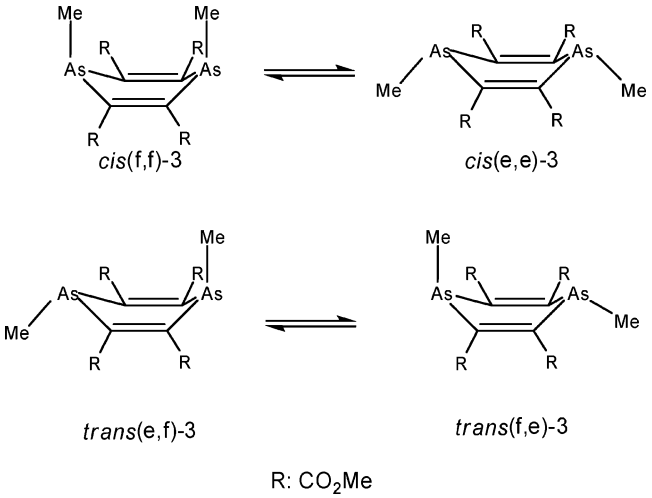
Experimental Section

Materials. Unless otherwise noted, all reagents and chemicals were purchased from commercial sources and used without further purification. Dehydrated benzene (water <30 ppm, Wako Pure Chemical Industries, Ltd.) was bubbled with a stream of nitrogen before use. 2,2′-Azobis(isobutyronitrile) (AIBN) was recrystallized from methanol. Dimethyl acetylenedicarboxylate (**2a**) and 2-ethynylpyridine (**2c**) were distilled before use.

Pentamethylcyclopentaarsine (1). 1 was prepared according to ref 9a. ^{1}H NMR (δ in $CDCl_3$, ppm): 1.63, 1.64, 1.67 (lit.[9a] 1.62, 1.63, 1.66).

Equipment. ^{1}H and ^{13}C NMR spectra were obtained using a JEOL JNM-EX270 instrument (270 and 67.5 MHz, respectively) for solutions in $CDCl_3$ and were referenced to $SiMe_4$ (TMS).

Chart 1. Possible Structures of the Isomers of 3a



1,4-Dihydro-1,4-dimethyl-2,3,5,6-tetrakis(methoxycarbonyl)-1,4-diarsinine (3a). Under a nitrogen atmosphere, a benzene solution (0.5 mL) of AIBN (5 mol %) was added to a refluxing benzene solution (4.5 mL) of dimethyl acetylenedicarboxylate (**2a**; 0.213 g, 1.5 mmol) and **1** (0.135 g, 0.30 mmol). After the mixture was refluxed for 15 h, the solvent was removed to yield a yellow solid. The obtained solid was dissolved in dichloromethane, and *n*-hexane was added to remove the oligomeric products as a red precipitate. **3a** was obtained by removal of the solvent from the *n*-hexane-soluble part, followed by recrystallization from acetonitrile to afford a colorless crystalline solid which was suitable for X-ray analysis (isolated yield 34%). $R_f = 0.10$ (CH_2Cl_2). Mp: 102−103 °C. ^{1}H NMR (δ in $CDCl_3$, ppm): 3.80 (s, 12H, CO_2CH_3), 1.50 (s, 6H, As−CH_3). ^{13}C NMR (δ in $CDCl_3$, ppm): 166.4 (CO_2CH_3), 145.2 (As*C*═*C*As), 52.6 (CO_2CH_3), 7.8 (As*C*H_3). HR FAB-MS (*m*/*z*): calcd for [$C_{14}H_{18}O_8As_2^+ - CHCl_3$], 463.9434; obsd, 463.9434; error, +0.0. Anal. Found: C, 36.1; H, 3.7. Calcd for $C_{14}H_{18}O_8As_2$: C, 36.2; H, 3.9.

1,4-Dihydro-1,4-dimethyl-2,5-bis(4-pyridyl)-1,4-diarsinine (3b). 3b was prepared as a colorless crystal in a fashion similar to that for **3a**, with **2a** being replaced by 4-ethynylpyridine (**2b**). Isolated yield: 30%. Mp: 178−180 °C. ^{1}H NMR (δ in $CDCl_3$, ppm): 8.58 (d, 4H, $J = 6$ Hz, 2-pyr *H*), 7.16 (d, 4H, $J = 6$ Hz, 3-pyr *H*), 6.91 (s, 2H, C═C*H*), 1.13 (s, 6H, AsCH_3). ^{13}C NMR (δ in $CDCl_3$, ppm): 149.9 (2-pyr *C*), 149.7 (pyr *C*═CH), 146.5 (4-pyr *C*), 136.9 (H*C*═C pyr), 121.6 (3-pyr *C*), 8.0 (As-CH_3). HR FAB-MS (*m*/*z*): calcd for [$C_{16}H_{17}N_2As_2^+ - CHCl_3$], 386.9823; obsd, 386.9826; error, +0.3.

Acknowledgment. We thank the 21st century COE program, COE for a United Approach to New Material Science, for supporting this work. We are indebted to Prof. Yoshihiro Matano (Department of Molecular Engineering, Kyoto University) for generous help with the X-ray crystallographic analysis.

Supporting Information Available: ^{1}H and ^{13}C NMR spectra of *cis*(e,e)-**3a**, the ^{1}H NMR spectrum of *cis*(e,e)-**3b**, and CIF files giving crystallographic data for *cis*(e,e)-**3a** and *cis*(e,e)-**3b**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM070080G