Supplementary Materials

Dithiol Aryl Arsenic Compounds as Potential Diagnostic and Therapeutic Radiopharmaceuticals

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Several dithioarylarsines were synthesized (literature modification developed)[32,33] and fully characterized, including their X-ray crystal structures.

Synthesis and Characterization of Additional Dithioarylarsines.

4-(1,3,2-dithiaarsolan-2-yl)aniline [$NH_2C_6H_4As(SCH_2CH_2S)$], ***S4***. *p*-Arsanilic acid (109.5 mg, 0.504 mmol) was dissolved in ethanol (95%, 20 mL) in a 100 mL round bottom flask equipped with a stir bar, and heated to 55 °C in a water bath. Aqueous ammonium mercaptoacetate (5.5 M, 458 µL, 2.52 mmol) was added, and heating continued while stirring vigorously. After 60 minutes, the flask was removed from heat and 1,2-ethane dithiol (47.5 mg, 42.4 µL, 0.504 mmol) was added. The resultant reaction mixture was stirred for 30 minutes, at which time water (~50 mL) was added until the reaction turned milky white. After standing overnight in the freezer (-15°C), crystalline product was isolated by vacuum filtration, washed with water, and dried *in vacuo*. X-ray quality crystals were obtained by slow evaporation from methanol. Yield: 60%, 151 mg**.** ^{1}H-NMR ($CDCl_3$; 500 MHz) δ ppm: 3.21 (m, 2H, SC**H$_2$**), 3.34 (m, 2H, SC**H$_2$**), 3.78 (s, 2H, N**H$_2$**), 6.66 (d, 2H, Ar**H**), 7.42 (d, 2H, Ar**H**). ^{13}C-NMR ($CDCl_3$; 125.8 MHz) δ ppm: 41.76 (**C**H$_2$), 115.06 (Ar**C)**, 131.49 (Ar**C)**, 132.27 (Ar**C)**, 147.73 (Ar**C)**. ESI/APCI MS (*m/z*) 259.90 (259.96 calcd for $[C_8H_{10}NS_2As]$ $(M+H)^+$). Elem. Anal. Calcd (found) for $C_8H_{10}NS_2As$: C, 37.07 (37.15): H, 3.89 (3.94); N, 5.40 (5.34); S, 24.74 (24.95).

2-(4-aminophenyl)-1,3,2-dithiaarsolane-4,5-dicarboxylic acid, diammonium salt $(NH_4)_2[NH_2C_6H_4As(SCH(COO)CH(COO)S)]$, ***S5***. *p*-Arsanilic acid (106.5 mg, 0.490 mmol), 5.5 M ammonium mercaptoacetate (419 µL, 2.30 mmol) and dimercaptosuccinic acid (DMSA; 84.6 mg, 0.464 mmol) in ethanol (95%, 20 mL) were reacted as described above for **S4**. A white precipitate began to form shortly after the addition of DMSA. The product was collected via vacuum filtration, washed with cold ethanol and cold diethyl ether, and dried *in vacuo*. Yield: 68%, 109.6 mg. ^{1}H NMR (D_2O; 500 MHz) δ ppm: 4.41 (s, 2H, SC**H**), 6.78 (d, 2H, Ar**H**), 7.49 (d, 2H, Ar**H**). ^{13}C NMR (CD_3OD + D_2O; 125.8 MHz) δ ppm: 64.82 (S**C**HCOOH), 116.77 (Ar**C**), 132.06 (Ar**C**), 133.0 (Ar**C**), 149.43 (Ar**C**), 176.85 (**C**OOH). ESI/APCI MS (*m/z*): 345.72 (345.92 calcd for $[C_8H_{10}NS_2As]$ $[M-H]^-$). Elem. Anal. Calcd (found) for $C_{10}H_{16}N_3O_4S_2As$: C, 31.50 (31.39); H, 4.23 (4.09); N, 11.02 (10.03); S, 16.82 (17.42).

*4-(1,3,2-dithiaarsinan-2-yl)aniline [$NH_2C_6H_4As(SCH_2CH_2CH_2S)$], **S6***. *p*-Arsanilic acid (101.4 mg, 0.467 mmol), 5.5 M ammonium mercaptoacetate (419 µL, 2.30 mmol) and 1,3-propane dithiol (49.7 mg, 46 µL, 0.46 mmol) in ethanol (95%; 20 mL) were reacted and isolated as described above for **S4**. X-ray quality crystals were obtained by slow evaporation from methanol. Yield: 80%, 100.6 mg. ^{1}H NMR ($CDCl_3$; 500 MHz) δ ppm: 1.93 (m, 1H, C**H$_2$**), 2.14 (m, 1H, C**H$_2$**), 2.72 (m, 2H, SC**H$_2$**), 2.90 (m, 2H, SC**H$_2$**), 6.78 (d, 2H, Ar**H**), 7.65 (d, 2H, Ar**H**). ^{13}C NMR ($CDCl_3$; 125.8 MHz) δ ppm: 26.57 (SCH_2**C**H_2), 28.84 (S**C**H_2), 115.78 (Ar**C**), 125.85 (Ar**C**), 133.93 (Ar**C**), 147.65 (Ar**C**). ESI/APCI MS (*m/z*): 314.58 (315.00 calcd for [$C_{11}H_{15}N_2S_2As$] [M+CH_3CN+H]$^+$). Elem. Anal. Calcd (found) for [$C_9H_{12}NS_2As$: C, 39.56 (38.80); H, 4.43 (4.33); N, 5.13 (4.94); S, 23.47 (23.05).

*2-phenyl-1,3,2-dithiaarsolane [$C_6H_5As(SCH_2CH_2S)$], **S7***. Phenyl arsonic acid (101.0 mg, 0.5 mmol), 5.5 M ammonium mercaptoacetate (2.48 mmol, 450 µL) and 1,2-ethane dithiol (46.6 mg, 41.7 µL, 0.495 mmol) in ethanol (95%, 20 mL) were reacted and isolated as above for **S4**. The desired product, a white solid, was collected via vacuum filtration, washed with water, and dried *in vacuo*. X-ray quality crystals were obtained by slow evaporation from methanol. Yield: 53%, 64.1 mg. ^{1}H NMR ($CDCl_3$; 500 MHz) δ ppm: 3.17 (m, 2H, SC**H$_2$**), 3.37 (m, 2H, SC**H$_2$**), 7.31 (t, 1H, *p*-Ar**H**), 7.36 (t, 2H, Ar**H**), 7.65 (d, 2H, Ar**H**). ^{13}C NMR ($CDCl_3$; 125.8 MHz) δ ppm: 41.97 (S**C**H_2**)**, 128.57 (Ar**C)**, 129.18 (Ar**C)**, 130.74 (Ar**C)**, 143.80 (Ar**C)**. ESI/APCI MS (*m/z*): 261.05 (260.94 calcd for [$C_8H_{10}S_2AsO$] [M+OH]$^+$). Elem. Anal. Calcd (found) for $C_8H_9S_2As$: C, 39.35 (39.56); H, 3.71 (3.73); S, 26.26 (26.39).

*2-phenyl-1,3,2-dithiaarsolane-4,5-dicarboxylic acid, diammonium salt $(NH_4)_2$[$C_6H_5As(SCH(COO)CH(COO)S)$], **S8***. Phenyl arsonic acid (101.2 mg, 0.5 mmol), 5.5 M ammonium mercaptoacetate (2.48 mmol, 450 µL), and dimercaptosuccinic acid (89.8 mg, 0.493 mmol) in ethanol (95%, 20 mL) were reacted as described above for **S4**. Water was not needed to initiate precipitation and thus was not added. The product was collected as a white solid by vacuum filtration, washed with cold acetone, and dried *in vacuo*. X-ray quality crystals were obtained by slow evaporation from a mixture of water and acetone. Yield: 78%, 127.8 mg. ^{1}H NMR (D_2O; 500 MHz) δ ppm: 4.15 (s,

2H, SC**H**), 7.44 (t, 1H, *p*-Ar**H**), 7.49 (d, 2H, Ar**H**), 7.84 (d, 2H, Ar**H**). ^{13}C NMR (CD_3OD + D_2O; 125.8 MHz) δ ppm: 64.80 (S**C**H), 129.53 (Ar**C)**, 130.06 (Ar**C)**, 131.69 (Ar**C)**, 144.53 (Ar**C)**, 176.42 (**C**OOH). ESI/APCI MS (*m/z*): 331.25 (330.92 calcd for $[C_{10}H_9O_4S_2As]$ $[M-H]^-$). Elem. Anal. Calcd (found) for $C_{10}H_{15}N_2O_4S_2As$: C, 32.79 (32.67); H, 4.13 (4.11); N, 7.65 (7.27); S, 17.51 (18.20).

2-phenyl-1,3,2-dithiaarsinane [$C_6H_5As(SCH_2CH_2CH_2S)$], ***S9***. Phenyl arsonic acid (99.8 mg, 0.494 mmol), 5.5 M ammonium mercaptoacetate (2.48 mmol, 450 µL), and 1,3-propane dithiol (53.6 mg, 49.7 µL, 0.495 mmol) in ethanol (95%, 20 mL) were reacted as above for **S4**. Following the water addition, the ethanol was removed by rotary evaporation to facilitate precipitation of the product, and the reaction mixture was placed in the freezer (-15 °C) for an hour. The product, a white solid, was isolated via vacuum filtration, washed with water, and dried *in vacuo*. X-ray quality crystals were obtained by slow evaporation from methanol. Yield: 45%, 57.5 mg. ^{1}H NMR ($CDCl_3$; 500 MHz) δ ppm: 1.94 (m, 1H, C**H$_2$**), 2.17 (m, 1H, C**H$_2$**), 2.69 (m, 2H SC**H$_2$**), 2.84 (m, 2H, SC**H$_2$**), 7.40 (t, 1H, *p*-Ar**H**), 7.49 (t, 2H, Ar**H**), 7.91 (d, 2H, Ar**H**). ^{13}C NMR ($CDCl_3$; 125.8 MHz) δ ppm: 26.11 (SCH_2**C**H_2), 28.49 (S**C**H_2), 129.16 (Ar**C)**, 129.36 (Ar**C)**, 132.56 (Ar**C)**, 138.73 (Ar**C)**. ESI/APCI MS (*m/z*): 275.02 (274.95 calcd for $[C_9H_{12}S_2AsO]$ $[M+OH]^+$). Elem. Anal. Calcd (found) for $C_9H_{11}S_2As$: C, 41.86 (41.62); H, 4.29 (4.09).

2-(4-nitrophenyl)-1,3,2-dithiaarsolane [$NO_2C_6H_4As(SCH_2CH_2S)$], ***S10***. *p*-Nitro phenyl arsonic acid (102 mg, 0.411 mmol), 5.5 M ammonium mercaptoacetate (2.02 mmol, 368 µL), and 1,2-ethane dithiol (38.1 mg, 34.0 µL, 0.411 mmol) in H_2O/EtOH (1:1; 10 mL) were reacted as described above for **S4**. The reaction mixture was removed from heat and 1,2-ethane dithiol in a 50/50 mix of ethanol and acetone (10 mL total) was added. After stirring for 30 minutes, organic solvents were removed via vacuum distillation and cooled to give the crude product as a light yellow precipitate. The solids were isolated via vacuum filtration, washed with cold water, and dried *in vacuo* to give the pure product. X-ray quality crystals were obtained by slow evaporation from methanol. Yield: 69%, 91.8 mg. ^{1}H NMR ($CDCl_3$; 500 MHz) δ ppm: 3.11 (m, 2H, SC**H$_2$**), 3.42 (m, 2H, SC**H$_2$**), 7.85 (d, 2H, Ar**H**), 8.17 (d, 2H, Ar**H**). ^{13}C NMR ($CDCl_3$; 125.8 MHz) δ ppm: 42.42 (S**C**H_2), 123.09 (Ar**C**), 131.81 (Ar**C**), 148.43 (Ar**C**), 153.31 (Ar**C**). ESI/APCI MS

(*m/z*): 287.93 (287.91 calcd for $[C_8H_8NO_2S_2As]$ $[M-H]^-$). Elem. Anal. Calcd (found) for $C_8H_8NO_2S_2As$: C, 33.22 (33.49); H, 2.79 (2.69); N, 4.84 (4.75); S, 22.17 (22.43).

2-(4-nitrophenyl)-1,3,2-dithiaarsolane-4,5-dicarboxylic acid, diammonium salt $(NH_4)_2[NO_2C_6H_4As(SCH(COO)CH(COO)S)]$, ***S11***. *p*-Nitro phenyl arsonic acid (100 mg, 0.405 mmol), 5.5 M ammonium mercaptoacetate (368 µL, 2.02 mmol), and dimercaptosuccinic acid (74.4 mg, 0.408 mmol) in EtOH/acetone (1:1; 10 mL) and H_2O (1 mL) were reacted as above for **S4**. A light yellow precipitate began to form shortly after the addition of DMSA. After 30 minutes, acetone (5 mL) was added to further precipitate the product. The reaction mixture was cooled to, -15 °C, and filtered via vacuum filtration. The solids were washed with acetone, diethyl ether, and dried *in vacuo* to obtain the product. Yield: 71%, 108.3 mg. ^{1}H NMR (D_2O/CD_3OD; 500 MHz) δ ppm: 4.31 (s, 2H, SC**H**), 8.04 (d, 2H, Ar**H)**, 8.22 (d, 2H, Ar**H**). ^{13}C NMR (CD_3OD + D_2O; 125.8 MHz) δ ppm: 65.51 (S**C**H), 123.79 (Ar**C**), 133.16 (Ar**C**), 149.46 (Ar**C**), 155.19 (Ar**C**), 176.19 (**C**OOH). ESI/APCI MS (*m/z*): 375.72 (375.89 calcd for $[C_{10}H_8NO_6S_2As]$ $[M-H]^-$). Elem. Anal. Calcd (found) for $C_{10}H_{14}N_3O_6S_2As \cdot CH_3CH_2OH$: C, 31.51 (31.34); H, 4.41 (4.27); N, 9.19 (9.04); S, 14.02 (14.54).

2-(4-nitrophenyl)-1,3,2-dithiaarsinane $[NO_2C_6H_4As(SCH_2CH_2CH_2S)]$, ***S12***. *p*-Nitro phenyl arsonic acid (103.7 mg, 0.402 mmol), 5.5 M ammonium mercaptoacetate (2.02 mmol, 368 µL) and 1,3-propane dithiol (43.8 mg, 40.7 µL, 0.405 mmol) in ethanol (95%, 20 mL) were reacted as above for **S4**. The product, a light yellow solid, precipitated upon removal of the ethanol by rotary evaporation. The solids were collected by vacuum filtration, washed with water, and dried *in vacuo*. X-ray quality crystals were obtained by slow evaporation from a 50/50 mixture of chloroform and acetonitrile. Yield: 66%, 80.5 mg. ^{1}H NMR ($CDCl_3$ d_1; 500 MHz) δ ppm: 1.97 (m, 1H, C$\mathbf{H_2}$), 2.18 (m, 1H, C$\mathbf{H_2}$), 2.72 (m, 4H, SC$\mathbf{H_2}$), 8.13 (d, 2H, Ar**H**), 8.21 (d, 2H, Ar**H**). ^{13}C NMR ($CDCl_3$ d_1; 125.8 MHz) δ ppm: 25.84 (**C**H_2), 27.77 (S**C**H_2), 123.87 (Ar**C**), 133.66 (Ar**C**), 148.65 (Ar**C**), 148.49 (Ar**C**). ESI/APCI MS (*m/z*): 302.69 (302.94 calcd for $[C_9H_{10}NO_2S_2As]$ $[M^{+\cdot}]$). Elem. Anal. Calcd (found) for $C_9H_{10}NO_2S_2As$: C, 35.65 (35.57); H, 3.32 (3.32); N, 4.62 (4.52); S, 21.15 (21.26).

Figure S1. ORTEP representation of (**S4**) (CCDC 1436762) with 50% probability ellipsoids.

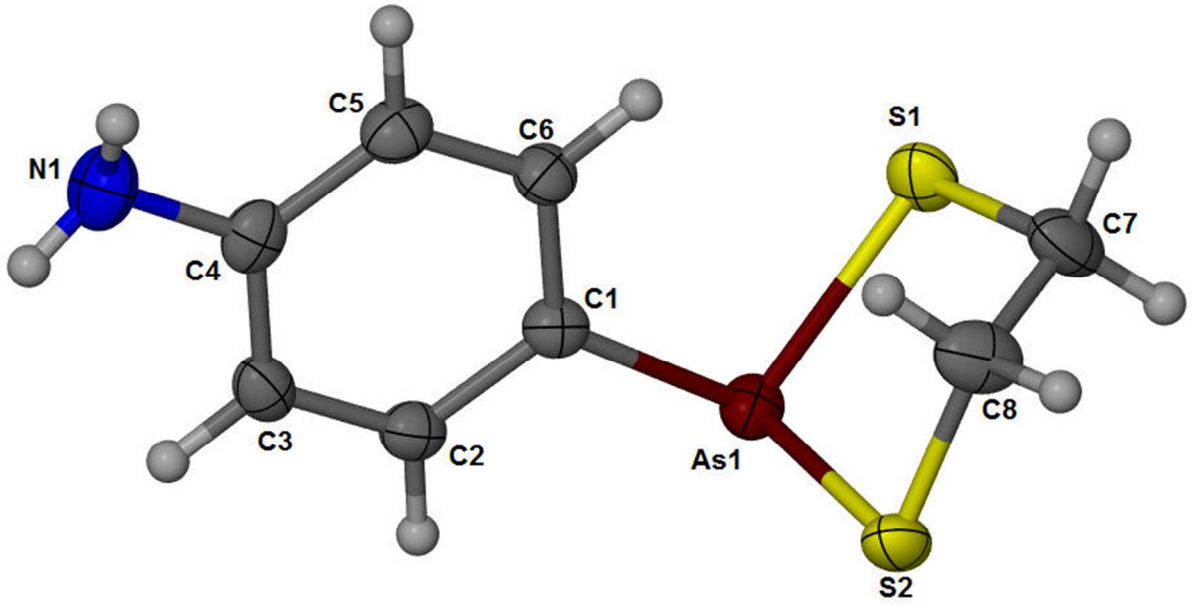

Figure S2. ORTEP representation of (**S6**) (CCDC# 1436763) with 50% probability ellipsoids.

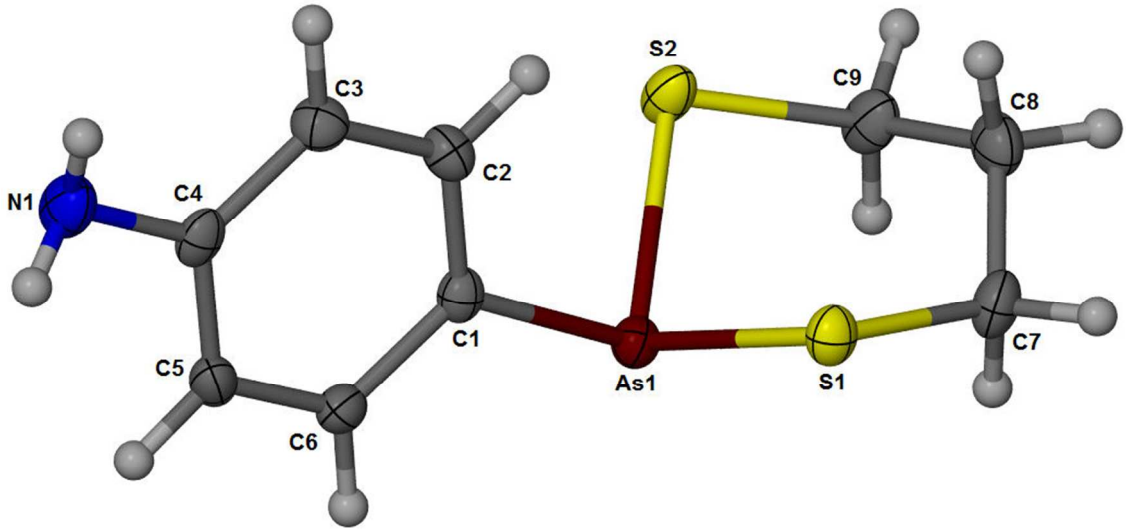

Figure S3. ORTEP representation of (**S7**) (CCDC# 1437260) with 50% probability ellipsoids.

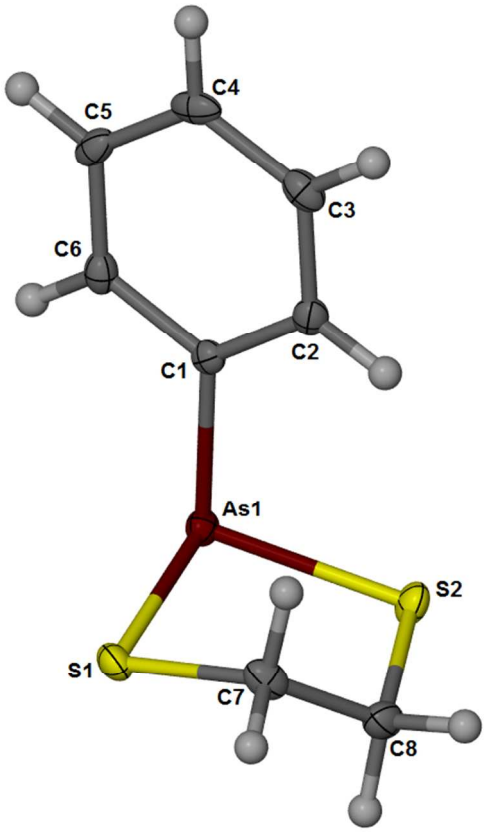

Figure S4. ORTEP representations of (**S8a** and **S8b**), obtained as the diammonium salt (omitted for clarity), (CCDC# 1436764) with 50% probability ellipsoids.

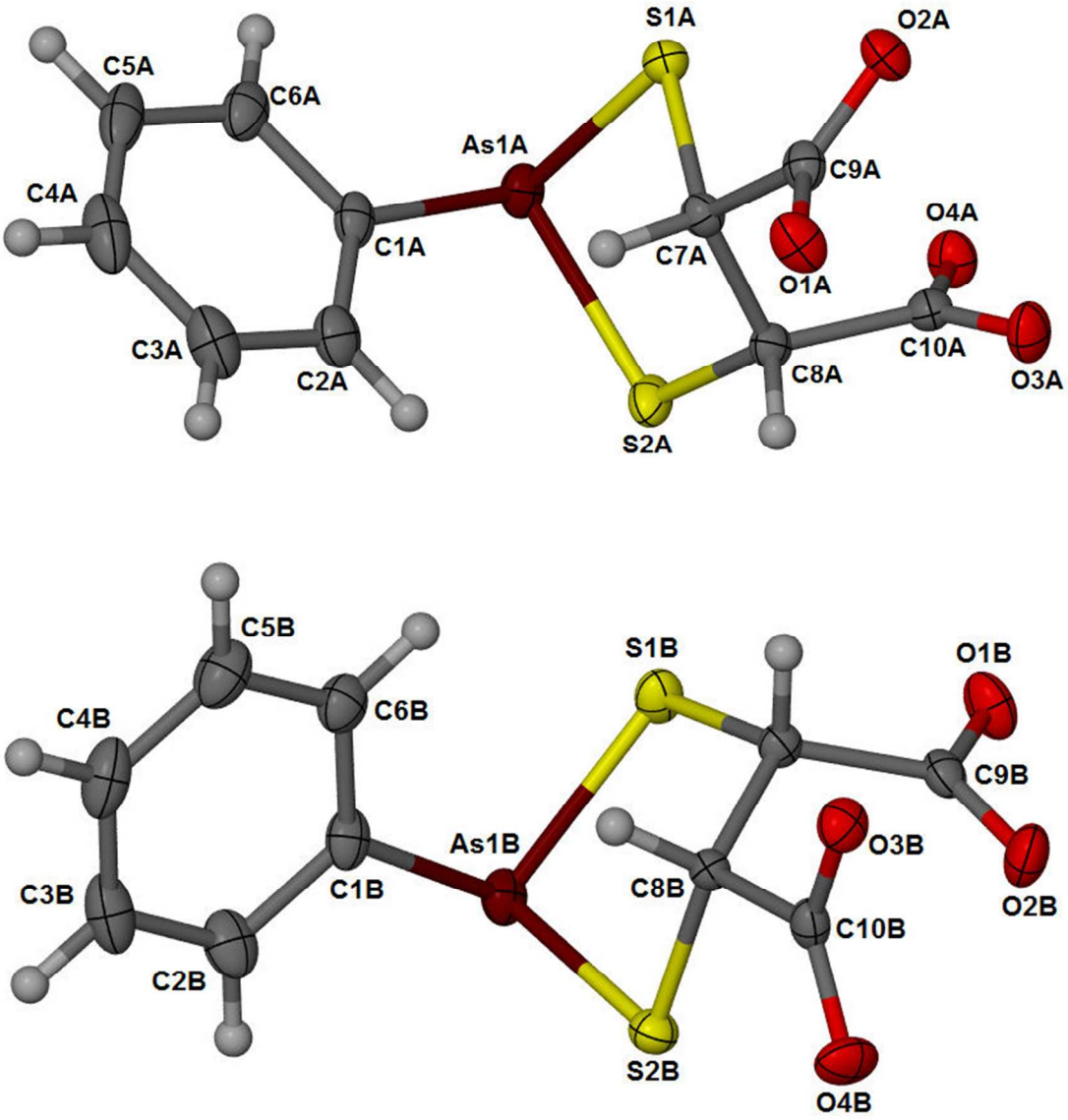

Figure S5. ORTEP representation of (**S9**) (CCDC# 1436765) with 50% probability ellipsoids.

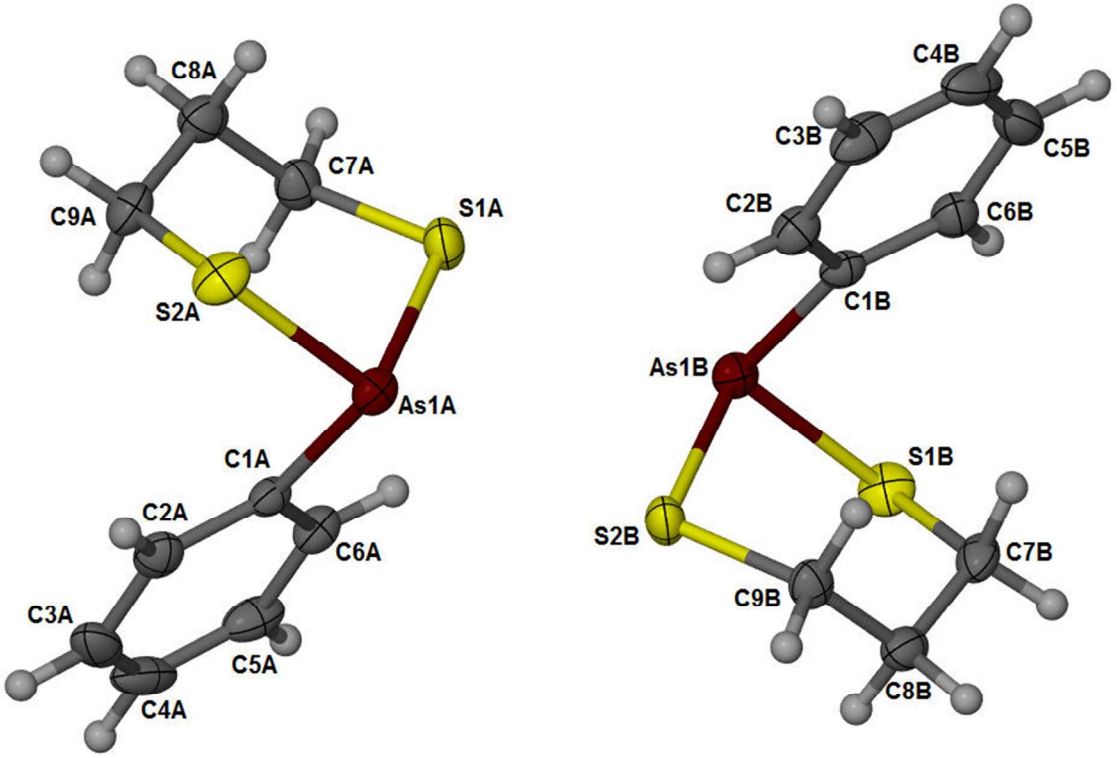

Figure S6. ORTEP representation of (**S10**) (CCDC# 1436766) with 50% probability ellipsoids.

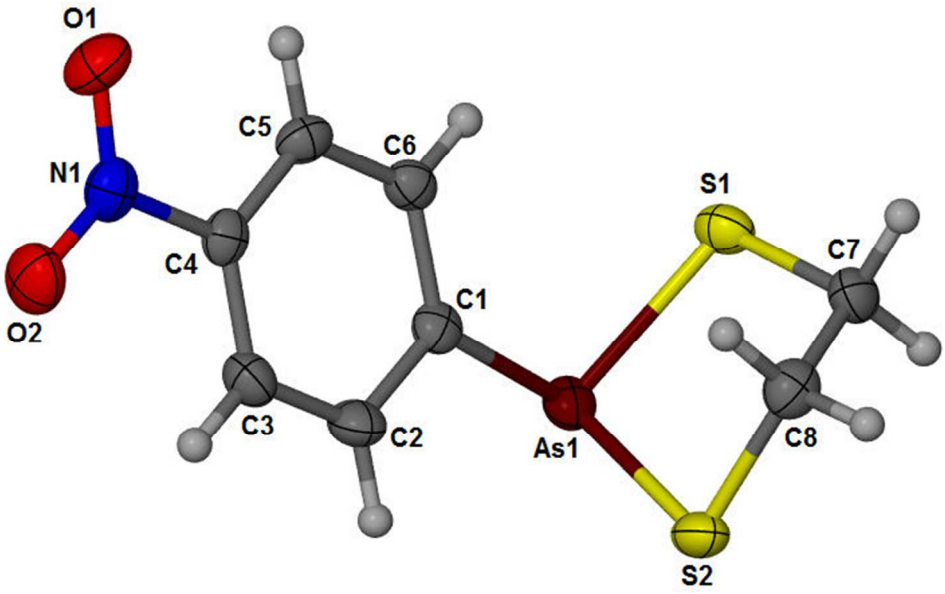

Figure S7. ORTEP representation of (**S12**) (CCDC# 1436767) with 50% probability ellipsoids.

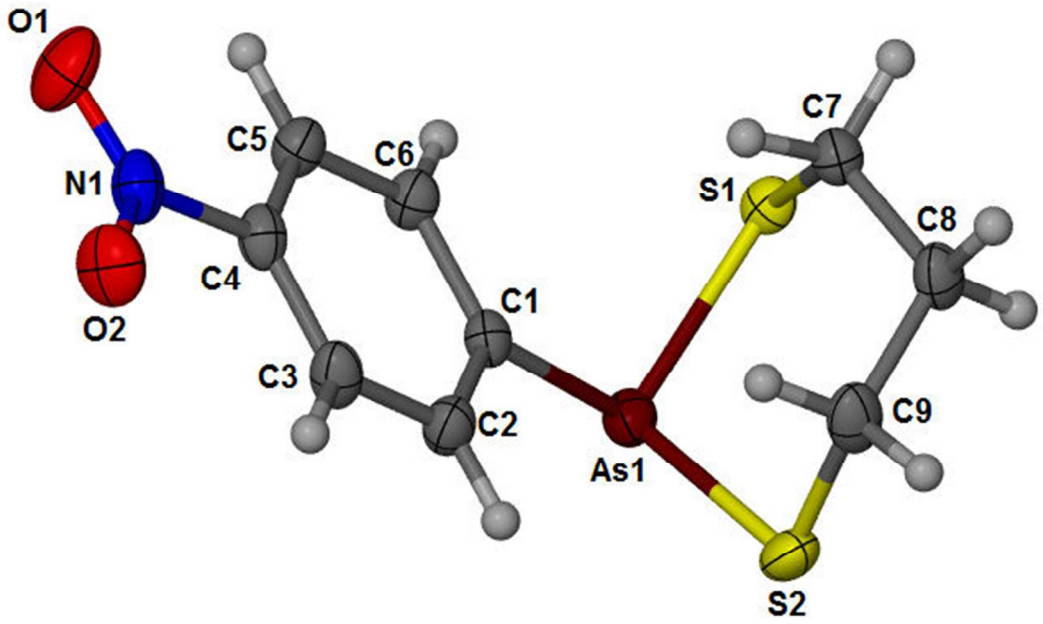

Table S1. ^{1}H- and ^{13}C-NMR alkyl dithiol proton and carbon chemical shifts for the aryldithioarsines (**1**-**3**, **S4**-**S12**) compared to the free ligands. Each methylene proton becomes unique on coordinating to the As(III). The aryl substituent is noted in parentheses following the compound number (**1**-**3**, **S4**-**S12**)

^{1}H-NMR Chemical Shifts (δ, ppm)			**^{13}C-NMR Chemical Shifts (δ, ppm)**		
	S**C**H_2	CH_2		S**C**H_2	**C**H_2
1,2-ethanedithiol	2.75		***1,2-ethanedithiol***	28.84	
1 (*p*-OEt)	3.19, 3.35		***1*** (*p*-OEt)	41.84	
S4 (*p*-NH_2)	3.21, 3.34		***S4*** (*p*-NH_2)	41.76	
S7 (*p*-H)	3.17, 3.37		***S7*** (*p*-H)	41.97	
S10 (*p*-NO_2)	3.11, 3.42		***S10*** (*p*-NO_2)	42.42	
DMSA	3.59		***DMSA***	41.23	
2 (*p*-OEt)	4.45		***2*** (*p*-OEt)	63.33	
S5 (*p*-NH_2)	4.41		***S5*** (*p*-NH_2)	64.82	
S8 (*p*-H)	4.15		***S8*** (*p*-H)	64.80	
S11 (*p*-NO_2)	4.31		***S11*** (*p*-NO_2)	65.51	
1,3-propanedithiol	2.68	1.91	***1,3-propanedithiol***	37.43	23.00
3 (*p*-OEt)	2.71, 2.87	2.14, 2.17	***3*** (*p*-OEt)	28.67	26.32
S6 (*p*-NH_2)	2.72, 2.90	1.92, 2.14	***S6*** (*p*-NH_2)	28.84	26.57
S9 (*p*-H)	2.69, 2.84	1.94, 2.17	***S9*** (*p*-H)	28.49	26.11
S12 (*p*-NO_2)	2.72	1.97, 2.18	***S12*** (*p*-NO_2)	27.62	25.68

Table S2. X-ray crystal data, data collection parameters, and refinement parameters for **S4**, **S6**-**S10 and S12**.

	S4	**S6**	**S7**	**S8a,b**	**S9a,b**	**S10**	**S12**
CCDC #	1436762	1436763	1437260	1436764	1436765	1436766	1436767
Formula	$C_8H_{10}AsNS_2$	$C_9H_{12}AsNS_2$	$C_8H_9AsS_2$	$C_{10}H_{17}AsN_2O_4S_2$	$C_9H_{11}AsS_2$	$C_8H_8AsNO_2S_2$	$C_9H_{10}AsNO_2S_2$
F.W.	259.21	273.24	244.19	384.3	258.22	289.19	303.22
Crystal System	Monoclinic	Orthorhombic	Orthorhombic	Triclinic	Monoclinic	Monoclinic	Monoclinic
Space Group	P 21/n	P 21 21 21	P 21 21 21	p $^{-}$1	P 21/n	P 21/n	C 2/c
a (Å)	12.346(5)	5.6626(9)	8.3948(7)	6.2774(9)	12.144(4)	11.234(3)	28.493(7)
b (Å)	6.184(2)	7.915(1)	9.8742(8)	16.094(2)	10.175(3)	6.3996(19)	7.1817(18)
c (Å)	13.254(5)	23.987(4)	11.0466(9)	16.875(2)	17.227(5)	14.612(4)	11.623(3)
α (°)	90	90	90	115.1390(10)	90	90	90
β (°)	95.594(4)	90	90	100.345(2)	106.308(3)	98.793(3)	107.713(3)
γ (°)	90	90	90	93.488(2)	90	90	90
V (Å ^{3})	1007.1(7)	1075.1(3)	915.67(13)	1500.2(4)	2043.1(1)	1038.1(5)	2265.6(10)
Z	4	4	4	4	8	4	8
$r_{calc.}$ g/cm^3	1.71	1.688	1.771	1.047	1.679	1.85	1.778
T, K	173(2)	173(2)	100(2)	173(2)	173(2)	173(2)	173(2)
μ, mm^{-1}	3.734	3.503	4.098	2.563	3.678	3.647	3.347
λ source (Å)	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073	0.71073
R(F)	0.0249	0.0163	0.0131	0.0256	0.0234	0.0227	0.0229
$R_w(F)^2$	0.0668	0.0413	0.0303	0.0615	0.0539	0.0491	0.0546
GoF	1.069	1.049	1.037	1.047	1.044	1.027	1.02

$R = (\Sigma||F_O| - |F_C||/\Sigma|F_O|)$. $R_W = [\Sigma\varpi(|F_O^2| - |F_C^2|)^2/\Sigma\varpi(|F_O^2|^2]^{1/2}$.

Table S3. Selected bond distances (Å) and angles (^{o}) for **S4**, **S6**-**S10 and 12**.

	S4	**S6**	**S7**	**S8**		**S9**		**S10**	**S12**
aryl	*p*-NH_2	*p*-NH_2	*p*-H	*p*-H		*p*-H		*p*-NO_2	*p*-NO_2
dithiol	ethyl	propyl	ethyl	DMSA		propyl		ethyl	propyl
				Molecule **a**	Molecule **b**	Molecule **a**	Molecule **b**		
As-S1	2.2516(1)	2.2452(5)	2.2394(6)	2.2418(5)	2.2470(6)	2.2310(8)	2.2301(7)	2.2369(8)	2.2279(7)
As-S2	2.2422(8)	2.2536(6)	2.2540(6)	2.2573(6)	2.2414(5)	2.2341(7)	2.2296(7)	2.2290(9)	2.2321(8)
As-C1	1.940(2)	1.940(2)	1.972(2)	1.9657(2)	1.9644(2)	1.9615(2)	1.9699(2)	1.986(2)	1.9712(2)
S1-As-S2	92.56(2)	97.27(2)	93.34(2)	92.480(2)	91.94(2)	99.28(3)	99.78(3)	93.91(2)	100.87(2)
S1-As-C1	100.75(6)	97.71(5)	100.29(6)	97.49(5)	101.28(6)	100.04(6)	99.76(6)	100.33(6)	98.53(6)
S2-As-C1	100.60(7)	97.05(6)	100.82(7)	100.68(6)	98.48(6)	99.91(6)	100.38(6)	98.99(6)	99.96(6)