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Syntheses of Arsinolipids: Non-isosteric Analogues of Phospholipids

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Reaction of alkaline benzenearsonous and 2,3-dihydroxypropylarsonous acids with *rac*-glycidol affords the corresponding arsinic acids, which after reduction with thiophenol are acylated with either fatty-acid chlorides/pyridine or fatty acids/dicyclohexylcarbodiimide/4-dimethylaminopyridine and oxidized with hydrogen peroxide to give the arsinolipids (*rac*-2,3-diacyloxypropyl)phenylarsinic and bis-(*rac*-2,3-diacyloxypropyl)arsinic acids. The latter is a non-isosteric analogue of bisphosphatidic acid.

Keywords: arsonous acids; arsinolipids; Auger reaction

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INTRODUCTION

Phosphonolipids are analogues of phospholipids, in having a P–C instead of a P–O bond.[1] Phosphonolipids derived from the parent 2-aminoethylphosphonic acid occur in nature[2] and have been synthesized in order to confirm the identity of the natural ones.[1] 'Unnatural' phosphonolipids, having the P–C bond on the 'diglyceride' side, have also been synthesized[1] for use in biophysical and biochemical studies.

True arsenic analogues of phospholipids have not been found in nature and their syntheses will be extremely difficult because the As–O bond is hydrolytically very unstable.[3] However, organoarsenic compounds, having an As–C bond, do exist in plants, microorganisms and animals (including Man).[4] They are especially abundant in marine organisms. The arsenic in these compounds is in the arsenic(V) state, e.g. $Me_3As^+CH_2COO^-$ (arsenobetaine) and $RMe_2As{=}O$. In some of them there are phospholipid components, e.g. glycerol phosphate, bisglycerol phosphate, and phosphatidyl glycerol.[4] In 1990 an arsenic-containing phosphonolipid, **1**, was prepared.[5] This lipid, too, contains arsenic(V), and replaces the nitrogen in the choline moiety.

Arsenic(V) differs from phosphorus(V) in size, the instability of its esters, and oxidizing ability; for example, arsenic(V) is reduced very easily by thiols to arsenic(III). We thought that by replacing the P in phosphonolipids with As we would produced compounds with interesting biochemical properties. We prepared arsonolipids **2** (*rac*, *R*, *S*) by acylating the mono-[6] or the bis-[7] tetrabutylammonium salts of *rac*[8,9] or optically active[7] 2,3-dihydroxypropylarsonic acids, **3**, with fatty-acid anhydrides. Better yields were obtained by acylating the thioarsenite **4** (obtained by reduction of **3** with thiophenol), with fatty-acid chlorides/pyridine, followed by oxidation.[10] These arsonolipids proved to be of value in elucidating the mechanism of action of phospholipase A_2[11] and they are potent non-competitive inhibitors of carbonic anhydrase, isozyme II.[12] The arsonolipids form liposomes either alone[7,10] or in the presence of phospholipids and/or cholesterol (D. Fatouros *et al.*, in preparation) and studies are under way to understand their properties. Also, the liposomes alone or loaded with drugs, acting as entry species, are being studied with healthy and cancer cells.

Since a mild way (i.e avoiding concentrated hydrochloric acid/sulphur dioxide) has been found for the reduction of arsonic acids to arsenoso compounds,[13] the way is now open for the synthesis of more complex arsenic-containing lipids, as well as other analogues of biochemically interesting molecules.

Herein we report on the synthesis of the arsinolipids *rac*-**5** and *rac*-**6**, starting from arsenosobenzene, **7a**, and arsenoso(*rac*-2,3-dihydroxypropane), **7b**.

For the lipids **2**, having the $—AsO_3H_2$ attached to

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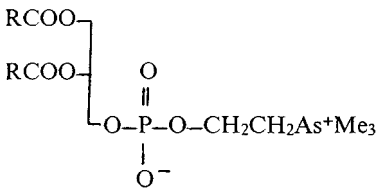

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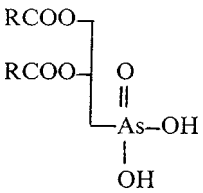

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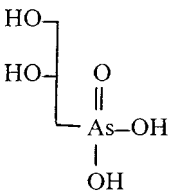

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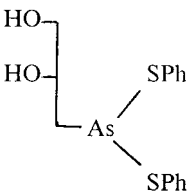

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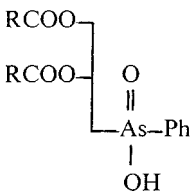

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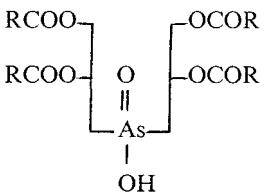


6

a 2,3-diacyloxypropyl group we proposed[8] the trivial name 'arsonolipids'. The name 'arsinolipids' can be given to lipids like **5** and **6** which have an $RAsO_2H$— attached to a 2,3-diacyloxypropyl group. The lipids **2**, **5** and **6** are non-isosteric[1] analogues of phospholipids because they do not have the C—*O*— As grouping. Isosteric arsonolipids with the C—CH_2—AsO_3H_2 group, have been prepared in very low overall yields.[14,15]

EXPERIMENTAL

Materials

Arsenosobenzene **7a** (m.p. 118–120 °C) and impure arsenoso(*rac*-2,3-dihydroxypropane) **7b** were prepared by reduction[13] of phenylarsonic acid (Aldrich) and *rac*-2,3-dihydroxypropylarsonic acid.[8,9] *rac*-Glycidol (b.p. 41 °C/1.5 mmHg) was prepared according to the literature.[16] Lauric and docosanoic acids (Aldrich), myristic acid (Serva), palmitic acid (Sigma) and stearic acid (Ferak) were used and the fatty-acid chlorides were prepared from redistilled thionyl chloride.[10] 1,3-Dicyclohexylcarbodiimide and 4-dimethylaminopyridine were from Aldrich. Carbon tetrachloride was dried over A_4 molecular sieves while dry chloroform was prepared just before use by distillation from phosphorus pentoxide. Silica gel 60 H (for TLC) was from Merck and silica gel Si 60 (for column chromatography) was from Serva.

Instruments and analyses

Thin-layer chromatography (TLC) was run on microslides. Visualization was achieved by spraying with 35% sulphuric acid and charring. IR spectra were obtained in KBr discs on a Perkin-Elmer model 16PC FT-IR spectrometer, and ^{1}H NMR spectra were obtained on Bruker models AMX or DPX Avance at 400 MHz. Melting points were obtained on an Electrothermal model IA9100 apparatus. Elemental analyses were done by CNRS, France.

(*rac*-2,3-Dihydroxypropyl)-phenylarsinic acid (9a)

Arsenosobenzene **7a** (1.0000 g, 5.95 mmol) was dissolved, at 50 °C, in 2 ml 6 M sodium hydroxide (12 mmol). To the stirred viscous solution, *rac*-glycidol (0.39 ml, 5.95 mmol) was added dropwise, during 1 h, at 50 °C. TLC (methanol) showed the salt of the product at R_f 0.29 and traces of glycerol at R_f 0.78, while in methanol/conc. ammonia (4:1) the product had R_f 0.40. After stirring at room temperature (RT) for 30 min, the solution was acidified to pH 2 with 6 M hydrochloric acid, evaporated (rotary, 40 °C) and dried *in vacuo* over phosphorus pentoxide for two days. The brownish solid was extracted, at RT, with methanol (4×4 ml) and the extracts were evaporated and dried *in vacuo* over phosphorus pentoxide for one day. The product (1.54 g) was an impure white foamy solid, decomposing at *ca* 65 °C, soluble in water, methanol and DMSO, and insoluble in chloroform, diethyl ether (Et_2O) and petroleum ether. The impurities were arsenosobenzene and methanol (from ^{1}H NMR) and traces of glycerol (by TLC). IR (KBr) (cm^{-1}): 3370 broad vs, 2550 broad vw, 1648 m, 1440 m, 1404 vw, 1090 ms, 1083 m (shoulder), 1045 m, 876 m, 803 m, 746 ms, 690 m, 464 m. The ^{1}H NMR spectrum in CH_3OH-d_4 or DMSO-d_6 was not well resolved for the propyl hydrogens.

(*rac*-2,3-Diacyloxypropyl)-phenylarsinic acids (5)

Using fatty acid chloride for acylation: general procedure

To a solution of impure **9a** (600 mg, 2.3 mmol if assumed to be pure **9a**) in methanol (5 ml), thiophenol (759 mg, 6.9 mmol) in methanol (3 ml) was added and stirred at RT for 1 h. Evaporation and drying *in vacuo* over phosphorus pentoxide for two days gave 1.176 g of the product **10a**, the by-product diphenyl disulphide and impurities [glycerol and $PhAs(SPh)_2$]. To the solid, dissolved in dry chloroform (8 ml), dry pyridine (0.46 ml, 5.75 mmol) was added and cooled at 0 °C. A solution of myristoyl chloride (1.417 g, 5.75 mmol) in dry chloroform (4 ml) was added dropwise, during 2 h, at 0 °C, and then it was left in the dark for six days. TLC (Et_2O/petroleum ether, 1:5) showed three 'spots': R_f 0.24 for RCOOH; R_f 0.64 for **11a**, triglyceride and $PhAs(SPh)_2$; R_f 0.95 for PhSSPh and RCOSPh. Evaporation gave a yellowish semi-solid to which Et_2O (10 ml) and water (5 ml) were added to give two clear, colourless phases. Addition of 0.38 ml of 30% hydrogen peroxide (3.45 mmol) and vigorous stirring for 2.5 h gave clear phases and a solid product at the interface. The water was syringed off and the Et_2O plus solid evaporated. The solid was dissolved in chloroform (3 ml) and applied to a column of silica gel (80 g) in ether. Elution with Et_2O (400 ml) removed the impurities, then chloroform/methanol (1:1; 10 ml) was added to push the product into the column (for otherwise it dissolves in chloroform/methanol, 20:3), and the product eluted with 200 ml chloroform/methanol (20:3). The pure product *rac*-**5** ($R = C_{13}H_{27}$) was a white solid, soluble in dichloromethane, chloroform, acetone or warm Et_2O, moderately soluble in ether, and sparingly soluble in petroleum ether. Data are shown in Table 1. IR (KBr) (cm^{-1}): 2920 vs, 2850 vs, 2700 broad vw, 1740 vs, 1468 m, 1457 mw, 1376 mw, 1256 mw, 1246 mw, 1209 m (shoulder), 1172 s, 1124 mw, 1094 mw, 882 mw, 744 m, 692 mw, 470 mw. ^{1}H NMR ($CDCl_3$), δ: 0.90 (s, 6H, C*H*$_3$), 1.27 and 1.45 (s and shoulder, 40H, (C*H*$_2$)$_{10}$), 1.60 (s, 4H, C*H*$_2$CH$_2$CO—), 2.30 (s, 4H, CH$_2$C*H*$_2$CO), 2.61 and 2.69 (s and broad, 2H, C*H*$_2$As), 3.21 (broad, 7H, As—O*H* and 3*H*$_2$O), 4.20 and 4.39 (s and s, 2H, RCOOC*H*$_2$), 5.42 (s, 1H, RCOOC*H*), 7.53 (s, 3H), 7.79 (s, 1.3H) and 8.09 (s, 0.7H) for —C$_6$*H*$_5$.

Using fatty acid/1,3-dicyclohexylcarbodiimide for acylation: general procedure

Impure **9a** (333 mg, 1.28 mmol if assumed to be pure **9a**) was converted, as described above, to **10a**. To this solid, docosanoic acid (957 mg, 2.82 mmol), 4-dimethylaminopyridine (32 mg, 0.25 mmol) and dry carbon tetrachloride (12 ml) were added. A solution of 1,3-dicyclohexylcarbodiimide (659 mg, 3.2 mmol) in dry carbon tetrachloride (2 ml) was added dropwise, during 15 min, at RT, and the system was stirred over a weekend. TLC (Et_2O) showed an intense spot at R_f 0.95–1.00

Table 1 Preparation, analytical and physical data of racemic arsinolipids 5 and 6

Lipid	Acylating agent[a]	Yield (%)	M.p. (°C)	Formula	mol wt	Analysis: Calcd Found C (%)	Analysis: Calcd Found H (%)	IR (KBr) (cm^{-1}) ν(As=0)	IR (KBr) (cm^{-1}) ν(As—O)[b]	^{1}H NMR δ	^{1}H NMR No. of H_2O per molecule
5, R = $C_{11}H_{23}$	A	68	51–53	$C_{33}H_{57}O_6As{\cdot}H_2O$	642.73	61.66 61.77	9.25 9.00	884	**744**, 724sh	6.50	0.5
5, R = $C_{13}H_{27}$	A	74	61–62	$C_{37}H_{65}O_6As$	680.81	65.27 64.97	9.62 9.74	882	**744**, 724	3.20	3
5, R = $C_{15}H_{31}$	B	60	72–73	$C_{41}H_{73}O_6As$	736.91	66.82 66.50	9.98 9.90	892	**746**, 722	2.60	6
5, R = $C_{17}H_{35}$	B	57	79–80	$C_{45}H_{81}O_6As$	793.01	68.15 68.01	10.29 10.31	892	**744**, 722	2.58	5
5, R = $C_{21}H_{43}$	B	56	88–89	$C_{53}H_{97}O_6As{\cdot}H_2O$	923.24	68.95 68.71	10.81 10.64	892	**744**, 722	2.15	9
6, R = $C_{11}H_{23}$	B	23	60–61	$C_{54}H_{103}O_{10}As{\cdot}H_2O$	1005.28	64.51 64.52	10.52 10.80	892	750sh, **728**	1.96 or 2.56	12 6
6, R = $C_{13}H_{27}$	B	25	69–70	$C_{62}H_{119}O_{10}As{\cdot}H_2O$	1117.59	66.63 66.76	10.91 10.77	892	754, **722**	1.96	9
6, R = $C_{15}H_{31}$	B	32	78–79	$C_{70}H_{135}O_{10}As{\cdot}H_2O$	1229.62	68.37 68.17	11.23 10.97	894	752, **722**	1.96	9
6, R = $C_{17}H_{35}$	B	43	88–89	$C_{78}H_{151}O_{10}As$	1323.81	70.76 70.89	11.49 11.62	894	754, **722**	1.14 1.71 1.95 3.49	3 3 2 1

[a] A, RCOCl/py; B, RCOOH/DCC/DMAP.
[b] The bold numbers indicate the stronger of the two bands.

due to PhSSPh, $PhAs(SPh)_2$, triglyceride and the product **11a**, and faint spots at R_f 0.72 for RCOOH and R_f 0.60 for acylated dicyclohexylurea (which gave a characteristic yellow colour before being charred). Filtration through Celite, washing with chloroform (12 ml), evaporation and drying *in vacuo* gave a solid which was oxidized by 0.18 ml of 30% hydrogen peroxide (1.92 mmol) in a biphasic Et_2O/H_2O (15 ml:7 ml) system. Isolation of the impure product and chromatography [silica gel (50 g) in Et_2O; elution with Et_2O (300 ml), chloroform/methanol (1:1; 10 ml), (see the preceding section) and chloroform/methanol (20:3; 400 ml)] as above gave the product *rac*-**5** ($R = C_{21}H_{43}$) (648 mg, 56%) as a white solid, soluble in chloroform, moderately soluble in warm Et_2O, and sparingly soluble in acetone. Data are shown in Table 1. The IR spectrum is similar to that of *rac*-**5** ($R = C_{13}H_{27}$), as is the ^{1}H NMR spectrum; in this case, nine water molecules resonate at δ 2.10–2.17.

Bis-(*rac*-2,3-dihydroxypropyl)arsinic acid (9b)

Impure[13] (contaminated with traces of $Ph_3P^+CH_2CH(OH)CH_2OH$, CH_3OH and silica gel) arsenoso(*rac*-2,3-dihydroxypropane) **7b** (141 mg, 0.85 mmol) was dissolved, at 50 °C, in 0.26 ml of 6.5 M sodium hydroxide (1.7 mmol) to give an opalescent yellowish solution. *rac*-Glycidol (0.06 ml, 0.85 mmol) was added dropwise, during 15 min, to the solution at 50 °C, and then stirred at RT for 30 min. TLC (MeOH/conc. NH_3, 4:1) showed the product (tailing spot at R_f 0.4) and traces of glycerol (R_f 0.75). The solution was acidified to pH 2 with 6 M hydrochloric acid, evaporated and dried *in vacuo* over phosphorus pentoxide for two days. The white, sticky solid was extracted with methanol (3×1 ml), the extracts evaporated and dried *in vacuo* over phosphorus pentoxide to give the impure product **9b** as a very hygroscopic white solid (275 mg, 219 mg expected), soluble in water and methanol. The product had the following impurities: traces of $SiO_2 \cdot xH_2O$ and $CH_2(OH)CH(OH)CH_2P^+Ph_3$ from the impure **7b**, glycerol and **3**, methanol and traces of sodium chloride. IR (neat) (cm^{-1}): 3356 broad vs, 2600 broad vw, 1648 m, 1457 m, 1401 m, 1088 s, 1053 s, 876 m, 793 mw (shoulder), 748 m, 699 w. ^{1}H NMR (D_2O), δ:2.56 (s, C*H*$_2$As), 3.51 (s, C*H*$_2$OH and glycerol), 4.16 (s, C*H*OH), 7.50 (m, $CH_2(OH)CH(OH)CH_2P^+$*Ph*$_3$).

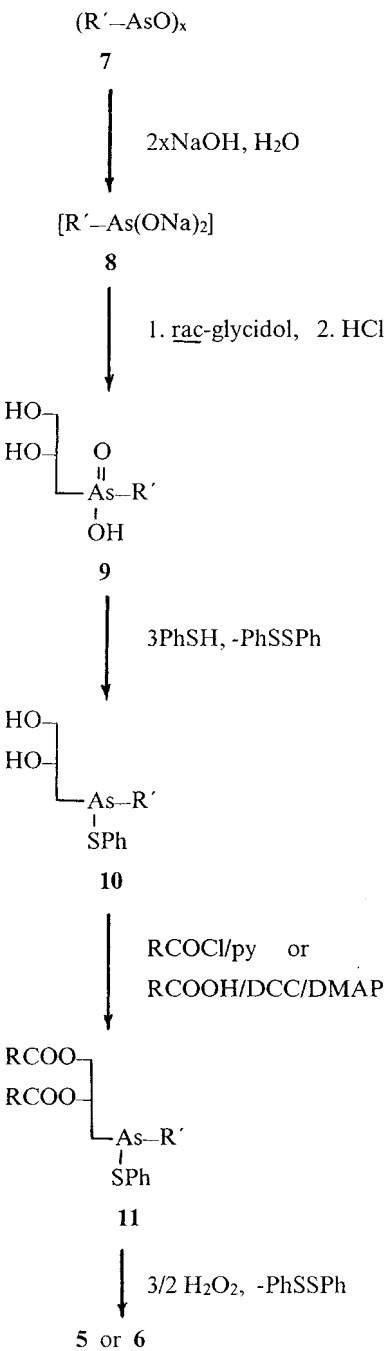
Phenyl ester of bis-(*rac*-2,3-dihydroxypropyl) thioarsinous acid (10b)

To the impure **9b** (270 mg, 0.85 mmol if assumed to be pure **9b**) dissolved in methanol (1 ml) to give an opalescent solution, thiophenol (280 mg, 2.55 mmol) dissolved in methanol (1 ml) was added and stirred at RT for 1 h. Evaporation and drying *in vacuo* gave a white solid from which the diphenyl disulphide was extracted by warm petroleum ether (4×2 ml). The gum was then extracted with boiling acetonitrile (3×2 ml). Removal of the solvent and drying gave the impure product **10b** (306 mg, 284 mg expected) as semi-solid crystals, soluble in methanol and moderately soluble in water. The product was contaminated by $CH_2(OH)CH(OH)CH_2P^+Ph_3$, the thioarsenite **4** and glycerol (by TLC and ^{1}H NMR). IR (neat) (cm^{-1}): 3418 broad vs, 3070 m, 2922 s, 2885 s, 1646 w, 1578 s, 1472 vs, 1436 vs, 1414 s, 1330 m, 1234 m, 1068 broad vs, 1045 vs, 926 w, 868 m, 742 vs, 692 vs. ^{1}H NMR (CH_3OH-d_4), δ:2.04 (s, C*H*$_2$As), 3.55 (s, C*H*$_2$OH and glycerol), 3.99 (s, C*H*OH), 7.4 (m, C_6H_5).

Bis-(*rac*-2,3-diacyloxypropyl)arsinic acids (6)

General procedure

Impure **10b** (388 mg, 1.16 mmol if assumed to be pure **10b**), stearic acid (1.4490 g, 5.1 mmol), and 4-dimethylaminopyridine (32 mg, 0.26 mmol) were dissolved in dry carbon tetrachloride (10 ml). To the opalescent solution was added, at RT, during 15 min a solution of 1,3-dicyclohexylcarbodiimide (1.195 g, 5.8 mmol) in dry carbon tetrachloride (2 ml) and the system was stirred at RT over a weekend. Filtration through Celite, washing with chloroform (8 ml), evaporation and drying gave a foamy white solid. TLC (Et_2O) showed an intense spot at R_f 0.95–1.00 due to triglyceride, esterified **4** and the product **11b**, and faint spots at R_f 0.70 for RCOOH, 0.50 for acylated dicyclohexylurea and ~0.1 for $CH_2(OCOR)CH(OCOR)CH_2$ P Ph_3. The solid was oxidized by vigorous stirring for 1 h at RT in a biphasic Et_2O/H_2O (20 ml/8 ml) system with 30% hydrogen peroxide (0.25 ml, 2.26 mmol). After centrifugation, the water was syringed off and the Et_2O plus solid product was evaporated and dried *in vacuo* to give 1.77 g of a white foamy solid. This, dissolved in chloroform/methanol (10:1; 3 ml) was chromatographed on silica gel (70 g) in Et_2O. Elution with Et_2O (550 ml), chloroform/

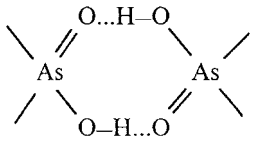


7-10 a. R′= Ph–
b. $CH_2(OH)CH(OH)CH_2$–

11a R′= Ph–
11b R′= $CH_2(OCOR)CH(OCOR)CH_2$–

Scheme 1

methanol (1:1; 10 ml) to push the product into the column, and chloroform/methanol (10:1; 500 ml) gave the pure product in the last eluent as per a white solid (663 mg, 43%), soluble in chloroform and insoluble in petroleum ether, Et_2O, acetone and methanol. Data are shown in Table 1. IR (KBr) (cm^{-1}): 2920 vs, 2850 vs, 2633 broad vw, 1742 s, 1626 m, 1576 mw, 1468 m, 1243 w, 1170 m, 1106



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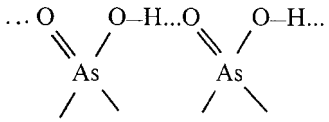

B

w, 894 w, 754 w, 722 w, 658 w, 614 w, ^{1}H NMR ($CDCl_3$), δ: 0.90 (s, 12H, C*H*$_3$), 1.27 (s, 112 H, 4 × (C*H*$_2$)$_{14}$), 1.62 (s, 8H, C*H*$_2$CH$_2$CO—), 2.33 (s, 8H, CH$_2$C*H*$_2$CO—), 2.57 (s, 4H, C*H*$_2$As), 4.10, 4.20, 4.42 (s, s, s, 4H, RCOOC*H*$_2$), 5.49 (s, 2H, RCOOC*H*). The water molecules resonate at δ = 1.14 (3H$_2$O), 1.72 (3H$_2$O), 1.95 (2H$_2$O) and 3.49 (1H$_2$O).

RESULTS AND DISCUSSION

The synthesis of the arsinolipids **5** and **6** (Scheme 1) starts from pure **7a** and impure **7b**. All reactions create by-products the nature of which is known, but they cannot easily or totally be removed at each step. Some of them are inert to thiols and some consume acylating reagents. However, chromatographic purification of the final products, **5** and **6**, was effective.

The Meyer reaction,[17] i.e. production of arsonic acids from aqueous alkaline arsenite and alkyl halide, is very fast and gives a high yield of **3** with the *water-soluble* glycidol,[7,10] although the concentration of the nucleophilic[18] species, AsO_3^{3-}, is extremely low. The Auger reaction[19] for the preparation of arsinic acids from aqueous alkaline arsonite and alkyl halide is analogous to the Meyer reaction. Because arsonous acids are very weak,[20] the concentration of the active species such as **8** should be low. However we found that **8** reacted fast and in high yields with the *water-soluble* glycidol to give **9**.

The reduction of As(V) in **9** to As(III) in **10** with thiophenol allows some purification of **10b** by extractions, but not so for **10a**, which has some solubility in petroleum ether. Compound **10** was acylated by fatty-acid chloride/pyridine, as in the case of **2**,[10] and by fatty acids/1,3-dicyclohexylcarbodiimide (DCC) in the presence of a catalytic amount of 4-dimethylaminopyridine.[21] In both cases we could not follow the complete acylation by TLC because of the impurities present.

During the oxidation of **11** by hydrogen peroxide in a biphasic Et_2O/water system[10] the long-chain arsinolipids **5** (R = $C_{15}H_{31}$–$C_{21}H_{43}$) and all **6** (R = $C_{11}H_{23}$–$C_{17}H_{35}$) precipitated at the interphase. Isolation and purification by recrystallizations was not as successful as in the case of arsonolipids **2**[6,7,10] because of finite solubilities of **5** and **6** in Et_2O and the co-precipitation of the (excess) fatty acids, but it was effected by column chromatography.

Given the complexity of the systems **10** to be acylated, the possible C–As and/or S–As bond fissions during the acylation and oxidation were not studied as they had been in the case of arsonolipids **2**.[10] The yields of arsinolipids **5** and **6** (Table 1) were about the same as those for arsonolipids **2**,[6,10] and those of 5 were better than those of 6. No difference in the yields of **5** was noted when the acylation was done by fatty-acid chlorides and by fatty acids/DCC, although the latter method was much faster.

The melting points of both arsinolipids, **5** and **6**, increased by *ca* 9 °C per CH_2CH_2 unit in the chains. In the racemic arsonolipids, **2**, an increase of *ca* 7 °C per CH_2CH_2 in the chains was observed.[6,10] The melting points of the lipids with the same acyl chains are in the order **2** > **6** > **5**, implying stronger hydrogen bonding of the head-group, —AsO_3H_2, in the arsonolipids **2** than in arsinolipids **5** and **6** which have an =AsO_2H head-group. The higher melting points of arsinolipids **6** compared with **5** should be attributed to stronger hydrophobic interactions of the former because they have four acyl chains per molecule whereas the latter have only two plus a phenyl group, which may weaken these hydrophobic interactions.

No differences in the mobilities of **2**, of **5** or of **6** with different fatty-acyl chains were observed by TLC. However, **2, 5** and **6** have different mobilities in TLC with various solvents: with $CHCl_3$/MeOH (10:1), R_f 0.10 for **2**, 0.45 for **5**, 0.42 and 0.53 for **6** (attributable to diastereomers) and with $CHCl_3$/AcOH (10:1)[10] R_f 0.28 for **2**, 0.45 for **5**, 0.67 for **6**.

Qualitative experiments showed that **2** dissolved in wet $CHCl_3$/MeOH (84:16) is more stable than **6**. After three days at RT, faint spots at R_f 0.17 and

0.33 ($CHCl_3$/MeOH, 10:1) appeared that were attributable to bis(lyso-**6**) and lyso-**6**, respectively, due to hydrolysis of fatty-acyl chain(s).

The stretching frequency of As=O in **9a** and **9b** is at 876 cm^{-1}, as it is in diphenylarsinic acid.[22] The As—O stretching vibration in diphenylarsinic acid is split (770 and 755 cm^{-1}) because of hydrogen bonding.[22] For both **9a** and **9b**, the ν(As—O) are found to be at ~800 and 747 cm^{-1}, implying different hydrogen-bonding patterns. For the arsinolipids **5** and **6** the ν(As=O) is somewhat broad, indicating association. The frequencies ν(As=O) and ν(As—O) and the different intensities of the ν(As—O) bands (Table 1) imply hydrogen bonding of different strengths, which we attribute to arrangements **A** and **B**.

The ^{1}H NMR spectrum of **7b** showed three peaks for the CH_2OH and two peaks for the CH_2As groups.[13] The product **9b** showed these absorptions at the expected δ values (3.51 and 2.56, respectively), which are the same as those found in the spectrum of **3**.[8] In the ^{1}H NMR spectrum of **10b** the CH_2As(III) moves to δ 2.04 in accordance with the lower electronegativity of As(III) than As(V).

All the lines in the ^{1}H NMR spectra, in $CDCl_3$, of the arsinolipids **5** and **6** are broad, probably indicating association. The RCOOCH_2 protons in **5** and **6**, belonging to the AB part of an ABX spin system, are not resolved. They resonate in two regions: 4.10–4.20 and 4.35–4.39. The RCOOCH_2 protons of optically active dipalmitoyl-lecithin and 1,2-dipalmitoylglycerol, but not of dipalmitoyl-3-phosphatidic acid, resonate in two regions[23] Similarly, the CH_2As protons are not resolved. For **5** they are found either at δ 2.63 and 2.69, or at 2.68, and for all **6** are at δ 2.56. Finally, the lipids **5** and **6** pick up water molecules (Table 1). These form weak hydrogen bonds, thus resonating at 1.14–2.60, or stronger hydrogen bonds, thus resonating at lower fields.[24]

The arsinolipids **5** and **6**, therefore, can absorb water molecules from the solvent or from the air (see Table 1).

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