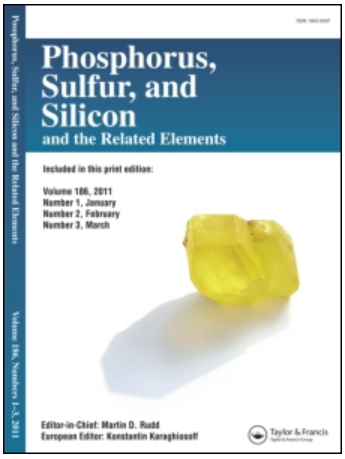

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rac-3,4-DIHYDROXYBUTYLARSONIC ACID: A KEY INTERMEDIATE FOR ISOSTERIC ARSONOLIPIDS

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rac-3,4-DIHYDROXYBUTYLARSONIC ACID: A KEY INTERMEDIATE FOR ISOSTERIC ARSONOLIPIDS

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Synthetic routes starting from 4-bromobut-1-ene and leading to *rac*-3,4-dihydroxybutylarsonic acid and diphenyl *rac*-3,4-dihydroxybutyldithioarsonite were explored. All of them gave overall yields 5–16%. Some properties of the free acid and its dilithium salt are described.

Key words: Arsonic acids, (diethylamino)chloroarsine, the Meyer reaction, salts of arsonic acids, cyclization of arsonic acids.

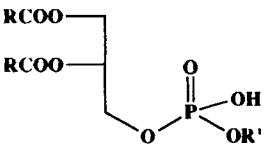
INTRODUCTION

Analogues of natural compounds have often proved useful as enzyme inhibitors and in chemotherapy. They can be selected for inability to undergo particular reactions of the natural metabolites. Hence analogues of phospholipids, **1**, can be made non-hydrolysable[1,2] in two ways. One is by removing the oxygen atom of the glycerol that is phosphorylated in **1**, to give non-isosteric analogues, **2**; the second is to replace this atom with a methylene group to give the isosteric analogues, **3**.

Simple replacement of the phosphorus of **1** by arsenic would give a rapidly hydrolysed compound (see Reference 3), since the larger size of the arsenic atom allows water to enter as a fifth ligand. Hence the first arsenic analogues[4–6] of **1** were made stable to hydrolysis by omitting the oxygen atom, to give the non-isosteric *rac*-, (*R*)- and (*S*)-analogues, **4**, and they are named 'arsonolipids.'[7] We now extend the range of analogues by working towards isosteric, non-hydrolysable analogues, **5**.

The synthesis of **5** can in principle be achieved *via* the key intermediate 3,4-dihydroxybutylarsonic acid **6**. This compound, being an analogue of glycerol 3-phosphate can be used in other biochemical studies.

We describe here the syntheses and chemical properties of *rac*-3,4-dihydroxybutylarsonic acid and its dilithium salt.



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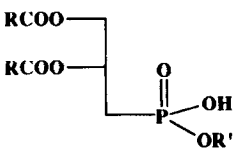

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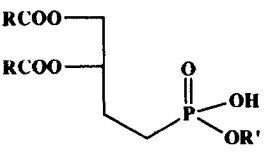

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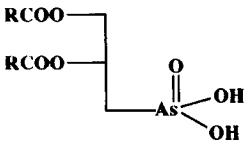

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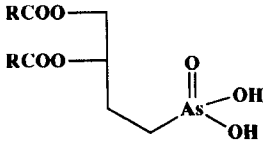

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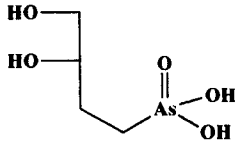


6

RESULTS AND DISCUSSION

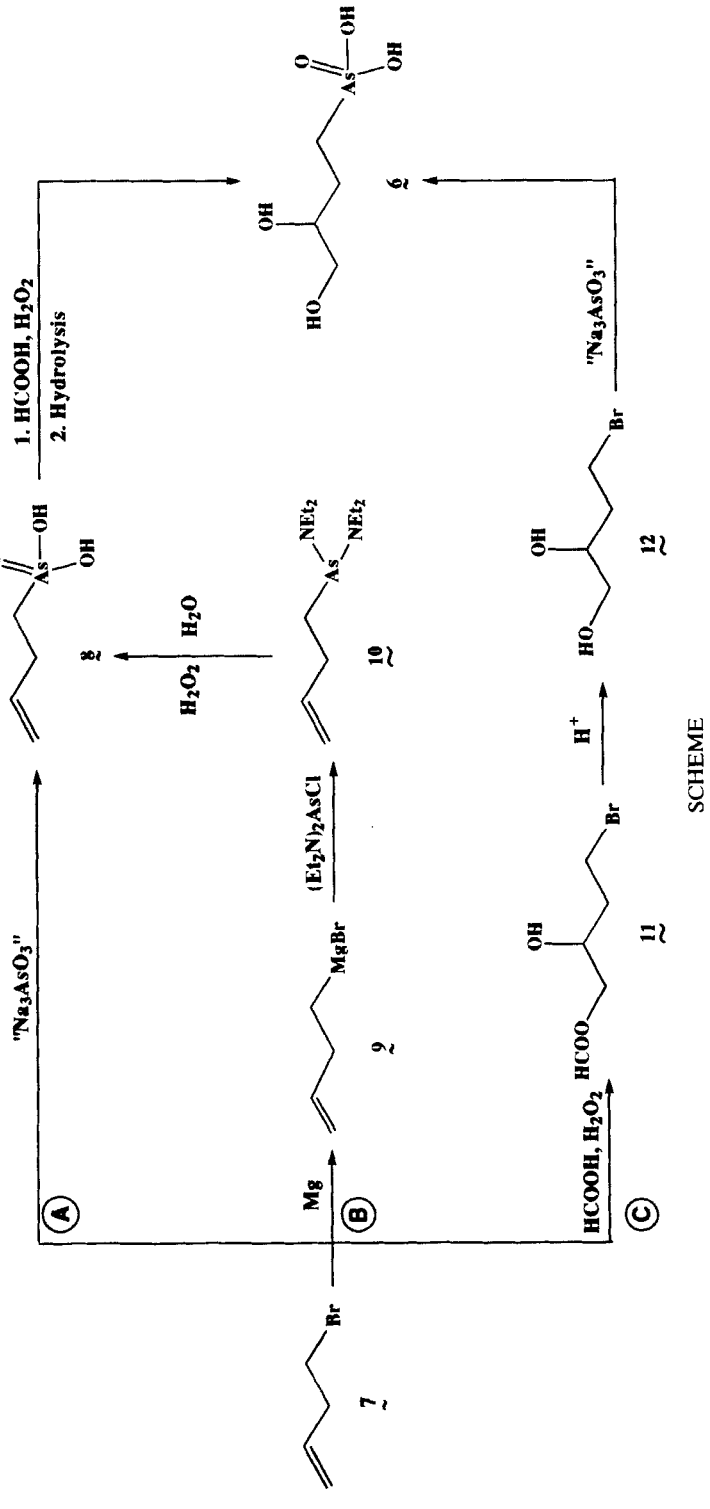
The synthesis of *rac*-**6** can, in principle, be achieved from 4-bromobut-1-ene, **7**, by three routes, Scheme.

Route A is a Meyer[8] reaction for displacing a halide ion with AsO_3^{3-}[9] to give an arsonic acid. Although simple in theory, the yield is very sensitive to the nature of the alkyl halide and the conditions of the reaction.[10,11] The effect of the insolubility of **7** in alkaline arsenite can be somewhat diminished by vigorous stirring, under reflux, to create a large surface between the organic and aqueous layers. Under these conditions the yield of **8** is about 10%.

Bis(diethylamino)chloroarsine[12] (Route B) reacted with the Grignard reagent **9** to give **10** which was oxidatively hydrolysed *in situ* to give **8** in 20% yield. While allylarsonic acid could not be epoxidized or hydroxylated,[4] but-3-enylarsonic acid, **8**, is converted by performic acid into **6** which, after ion exchange chromatography, is isolated as the dilithium salt in *ca* 50% yield. Some C—As bond fission occurred during the epoxidation of **8**, since arsenate was detected, but the phenomenon was not further investigated.

3,4-Dihydroxybutyl bromide, **12**, is a key intermediate to **6** *via* route C. The bromide could be obtained in optically active form[13] but the racemic mixture was obtained[14,15] from **7** and purified by column chromatography (see experimental). Pure **12** is heat labile.[15] It can be stored at −20°C for a few days but it gives a new spot on TLC, just above its own, which was identified as 3-hydroxytetrahydrofuran, **13**.[14]

Since tetramethylene chlorohydrin is cyclized rapidly even in water (with a half-life of 5–6 h at 50°C[16]), and faster in alkali, we thought that **12** was unlikely to undergo the Meyer reaction. We therefore tried it on partially protected (e.g. **11** and **14**) and fully protected (e.g. **15**) **12**.



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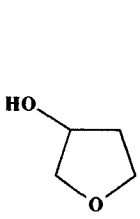

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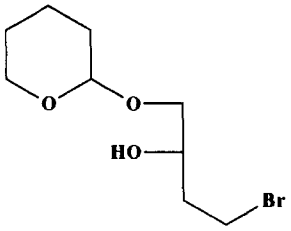

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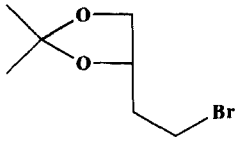


15

The new compounds **14** and **15** were prepared chromatographically pure in 60% and 38% yields respectively. These compounds, as well as **12**,[14,15] were unstable to storage and we could not obtain satisfactory elemental analyses.

The Meyer reaction of **11**, **14** and **15** under various conditions gave at best 11–13%, 26–33% and 18% consumption of As(III) respectively (titrimetric analysis).

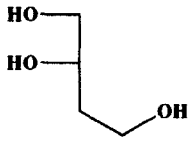
In view of the low overall yields with these substrates we studied the Meyer reaction with the hydrophilic **12** in order to find the conditions under which the nucleophilic displacement of —Br by AsO_3^{3-} will compete favourably with cyclization and with attack by HO^-. Best results were obtained a) in the absence of methanol as cosolvent, possibly because methanol diminished the concentration of the active species,[9] AsO_3^{3-}, b) in the presence of NaOH since it suppresses the hydrolysis of AsO_3^{3-},[17] and c) at 25°C, since higher temperatures seem to favour the production of **13** and **16** as opposed to **6**.

The *rac*-**6** obtained by route C was always contaminated with As_2O_3, **16**, and NaBr. One purification by ion exchange is described below under route B, but it can also be purified and characterized as the thioarsenite **17** because the latter can also be used for the synthesis of arsonolipids **5** using the procedure developed for the non-isosteric arsonolipids **4**.[6] The reduction of **6** to **17** was fast and quantitative but **17** could not be isolated entirely pure. It contained traces of **16** and very small amounts of diphenyldisulfide and triphenyl trithioarsenite,[18,19], $(PhS)_3As$. The latter is produced from the reaction of thiophenol with traces of arsenous acid (S. V. Serves *et al.*, manuscript in preparation). The overall yield of **17** was 26% on As(III) or 13% on **12**.

The oxidation of **17** with H_2O_2 in a biphasic system $H_2O/CHCl_3$ did not give **6** quantitatively (although diphenyl 2,3-dihydroxypropyldithioarsonite,[6] $HOCH_2CHOHCH_2As(SPh)_2$, used as a control, was quantitatively oxidized). Some C—As bond fission occurred because we detected 10–15% arsenate in **6**. Also, some "**6**" was retained in the organic phase presumably as cyclic derivative(s), which we could not isolate in pure state.

The free acid **6** (contaminated with H_3AsO_4) is a hygroscopic white solid which cyclizes by losing water on prolong drying in vacuo or by heating at 110°C. The cyclization can be detected by chemical means, i.e. reaction with thiophenol does not give **17** (TLC analysis), but not by TLC (MeOH/conc. NH_3) because the aqueous base converts it back into the open form, **6**. Its IR spectrum is qualitatively similar to that of 2,3-dihydroxypropylarsonic acid.[7]

The dilithium salt of **6**, obtained anhydrous, is a white feebly hygroscopic powder which does not melt up to 280°C. It is soluble in water and very slightly soluble in



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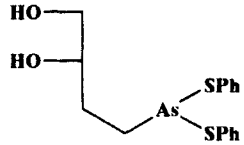

17

DMSO. Its IR spectrum (KBr pellet) shows a strong, broad absorption centered at 3386 cm^{-1} due to —OH groups and a very strong relatively sharp absorption at 848 cm^{-1} due to As=O in $—As(O)O_2^{2-}$ (see also Reference 7).

The contaminated **17** is an off-white gum soluble in $CHCl_3$ and insoluble in pentane. Its IR spectrum is qualitatively similar to that of diphenyl *rac*-2,3-dihydroxypropyldithioarsonite[7] and shows mainly the aromatic ring vibrations.

EXPERIMENTAL

4-Bromobut-1-ene (Aldrich) was used without further purification. 3,4-Dihydro-2*H*-pyran (Aldrich) was distilled and kept at −20°C. Dioxane was used without further purification. Anhydrous diethyl ether and ethanol were kept over A4 molecular sieves. Arsenic trichloride was prepared in 60% yield from arsenic trioxide and concentrated hydrochloric acid. Bis(diethylamino)chloroarsine was prepared according to McBrearty *et al.*[12] Silica gel Si60 (Serva) and Amberlite GC400 (BDH) were used for column chromatography and silica gel H (Merck) for thin layer chromatography (run on microslides). Visualization was effected by spraying with 35% H_2SO_4 and charring. The IR and ^{1}H-NMR spectra were obtained using a Perkin Elmer model 16PC FT-IR and a Varian model T-60A instruments respectively. Paper electrophoresis was performed on papers cooled by immersion in white spirit, in the system of Ambler.[20] Arsenic trioxide was determined titrimetrically in buffered, with $NaHCO_3$, solution with standard iodine solution.[21a] Test for arsenic acid was done using magnesia mixture.[21b] The arsenic in the organoarsenic compounds was determined after wet digestion with concentrated sulfuric acid and hydrogen peroxide.[22] Elemental analyses were done by the Chemical Laboratory of Cambridge University and by C.N.R.S., Vernaison, France.

ROUTE A: But-3-enylarsonic acid, **8.** Arsenic(III) oxide (15 g, 75 mmol) and NaOH (18 g, 0.45 mol) were dissolved in 20 ml of water. 4-Bromobut-1-ene (13.5 g, 0.1 mol) was added and the mixture was boiled under reflux with vigorous stirring for one week. It was cooled, diluted to about 100 ml with water, and adjusted to pH 8.5 with conc.HCl solution. Unreacted arsenic(III) oxide that precipitated was filtered off, the residue was adjusted to pH 3.5 with conc.HCl, and concentrated to about 50 ml. It was then extracted with 10 × 150 ml portions of ethyl acetate. The combined extracts were dried with sodium sulfate and evaporated to dryness to give the product **8** as a syrup. Paper electrophoresis showed the presence of a single arsonic acid, with a mobility consistent with but-3-enylarsonic acid **8**. The yield was 2 g (11%).

ROUTE B: But-3-enylarsonic acid, **8.** Magnesium turnings (3 g) and a few crystals of I_2 were placed in a 500 ml dry round bottom flask and heated over a Bunsen burner. After cooling, a few drops of Et_2O were added. To the effervescent mixture, 10 ml of Et_2O were added and then a solution of 10 ml (13,3 g, 0.1 mol) of 4-bromobut-1-ene in Et_2O (50 ml) was added portionwise so as to keep the mixture refluxing gently. The mixture was then refluxed for a further 30 min. To the refluxing solution of the Grignard reagent, **9**, $(Et_2N)_2AsCl$ (20 g) was added portionwise and the mixture refluxed for a further 1 h. Ether was removed by rotary evaporation, and 100 ml of water was added in portions with cooling to the remaining solid. Hydrogen peroxide (30%) was then added dropwise while cooling until there was no more increase in temperature. After stirring for 1 h at 25°C, the mixture was filtered. The filtrate was applied to a column (35 cm × 3 cm) of the strongly basic resin Amberlite GC400 in the acetate form, and the column was washed with two column volumes of water. The product was eluted with one litre of 1 M acetic acid. The solution was evaporated to dryness (rotary, <40°C) to give 4.0 g (20%) of **8** as a syrup.

rac-3,4-Dihydroxybutylarsonic acid, **6.** To a cold solution of the arsonic acid **8** (4.0 g, 22 mmol) in 90 ml of 98% formic acid in a 500 ml round bottom flask, 30 ml of hydrogen peroxide (100 volume, 30%)

were added, and the solution was stirred in an ice bath for 3 h. The reaction was followed by paper electrophoresis (on 3 MM Whatman paper, cooled in white spirit, at 110 V/cm at pH 3.5 for 15 min detecting arsonic acids with $FeCl_3$ and sulfosalicylic acid[23]). Although there was little difference in mobility between reactant and product, disappearance of the unsaturated acid, **8**, could be detected by spraying the dried paper with aqueous $KMnO_4$ (5 g/L) since **8** alone decolorized the permanganate; the reaction was usually complete in 3 h. Excess H_2O_2 was destroyed with a few crystals of I_2 and the solution was passed through a column of 35 cm × 3 cm of the strongly basic resin Amberlite GC400 (acetate form). The sample was washed through with 180 ml of water, and the product displaced by washing with 1 L of 1 M acetic acid (the water removed arsenite, and arsenate remained on the column from which it could be eluted in 10% formic acid). This solution was evaporated to dryness. The product was converted into its dilithium salt by dissolving in water and adjusting with 2 M LiOH to pH 11. Evaporation to dryness gave a white fluffy sample which was dissolved in water (15 ml) and crystallized on addition of methanol. Yield 2,4 g (53%). Elemental analysis gave: C 20.7, H 3.9%; $C_4H_9AsLi_2O_5$ requires C 21.3, H, 4.0%. The salt does not melt up to 280°C. It is soluble in H_2O, slightly soluble in DMSO and insoluble in MeOH, Et_2O and CH_2Cl_2. IR(KBr): 3386 broad, s, 2926 m, 1420 m, 1096 m, 848 vs, 522 s. ^{1}H-NMR (D_2O, DSS): 1.87 (broad singlet, 4H, $C\underline{H}_2C\underline{H}_2As$), 3.60 (m, 3H, $C\underline{H}_2(OH)C\underline{H}(OH)$).

ROUTE C: Formic ester(s) of rac-3,4-dihydroxybutyl bromide, **11.** The hydroxylation of **7** (see also References 14 and 15) by 30% aqueous hydrogen peroxide in 85% formic acid at 25°C gave, after removal of excess reagents, pale yellow to pale orange oils which retained traces of formic acid even after prolonged drying in vacuo. TLC analysis ($CHCl_3$/MeOH 20:1 v/v) revealed that they were composed of diester (R_f 0.76), monoester **11** (R_f 0.55) and diol **12** (R_f 0.27). **13** (R_f 0.33) was not detected. The mixture is soluble in CCl_4 and MeOH but sparingly soluble in H_2O. Mixtures with higher content of **11** (by TLC and IR) were used in the Meyer reaction.

rac-3,4-Dihydroxybutyl bromide, **12.** The crude ester mixture from the hydroxylation of 0.05 mol 4-bromobut-1-ene was dissolved in 50 ml methanol and 1.5 ml concentrated hydrochloric acid was added. The solution was stirred in the dark at 25°C till TLC ($CHCl_3$/MeOH 20:1) showed complete disappearance of the spots at R_f 0.76 and 0.55 (~2–3 h). Removal of solvent (rotary <35°C) afforded 10.2 g of product as pale yellow oil, pure by TLC ($CHCl_3$/MeOH 20:1, R_f 0.30) but contaminated by water. [In some preparations another small spot was seen at R_f 0.33 which is its cyclized product **13**]. The oil was chromatographed on silica gel (55 g) column eluting with $CHCl_3$/MeOH 20:1 v/v. Yield 92% of pale yellow oil, n_D^{35} 1.5038. IR (neat): 3300 broad. ^{1}H-NMR($CDCl_3$) δ: 2.00 (m, 2H, —$C\underline{H}_2$—), 3.60 (m, 4H, —$C\underline{H}_2$Br, —$C\underline{H}_2$OH), 3.90 (m, 1H, $C\underline{H}$—OH). Since the compound is unstable[15] we did not obtain elemental analysis. Purified **12** was used for the preparations of **14** and **15** but crude **12** was used for the Meyer reaction. When 48% aqueous HBr was used as catalyst the product was an orange oil.

Tetrahydropyranyl ether of rac-3,4-dihydroxybutyl bromide, **14.** 4.45 g (26 mmol) **12** (pure by TLC) and 93 mg (0.49 mmol) *p*-toluenesulfonic acid monohydrate were dissolved in 50 ml of dioxane. A solution of 2.40 g (28.6 mmol) of redistilled 3,4-dihydro-2*H*-pyran in 15 ml dioxane was added in the dark during 6 h and then the solution was stirred overnight. TLC (Et_2O/hexane 1:1) showed the product, R_f 0.50, and small amounts of fully blocked **12**, R_f 0.75, and **13** plus unreacted **12**, R_f 0.05. The catalyst was neutralized with 0.49 mmol aq. NaOH, the solvent removed (rotary) and the orange oil dried in vacuo, giving 5.95 g (expected 6.50 g) impure product. 1.20 g of it was chromatographed (in the dark) on 25 g silica gel eluting with $CHCl_3$/MeOH 40:1. The product, **14**, 0.717 g (61% yield) was a colorless oil. IR (neat): 3434 mw (broad), 2932 s, 2866 ms, 1130 s, 1078 s, 1032 s. The product was highly unstable (see results and discussion). After two days at +4°C, TLC (Et_2O/hexane 1:1) showed additional spots at R_f 0.75, 0.05 and 0.16 (probably **13**). Decomposition, but to a lesser extent, was observed with fully blocked **14**.

Isopropylidene ketal of rac-3,4-dihydroxybutyl bromide, **15.** 5.07 g (0.3 mmol) **12** (pure by TLC), 9 ml (1.2 mmol) acetone (dried over A4), 90 mg *p*-toluenesulfonic acid monohydrate and 50 ml of hexane were refluxed for 20 h in a Dean-and-Stark apparatus. The system was throughout heterogeneous and became brown due to decomposition of **12**. TLC ($CHCl_3$) showed the product, **15**, R_f 0.79 and **12**, R_f 0.04. After cooling at room temperature, the catalyst was neutralized with freshly fused sodium acetate and evaporated (rotary) to give a dark red-to-brown oil which was dissolved in Et_2O, decolorized with charcoal, and concentrated to give a yellow solution. This was chromatographed on 15 g silica gel eluting with $CHCl_3$. The product **15**, 2.36 g (38%) was a yellow oil, pure by TLC. n_D^{25} 1.4684. IR (neat): 2986 m, 1372 m, 1214 m, 1068 s, 848 m. ^{1}H-NMR(CCl_4) δ: 1,1 (d, J = 3 Hz, 6H, $\underline{Me}_2C$), 2.05 (q, J = 6 Hz, 2H, —$C\underline{H}_2$—), 3.40 (t, J = 6 Hz, 2H, —$C\underline{H}_2$Br), 4.10 (m, 3H, —$C\underline{H}_2$OCMe$_2$, —$C\underline{H}$OCMe$_2$). The compound did not give consistent elemental analyses, probably because it was unstable.

Diphenyl rac-3,4-dihydroxybutyldithioarsonite, **17.** To a solution of 0.495 g (2.5 mmol) As_2O_3 in 1.54 ml 13 M NaOH (15 mmol) was added dropwise during 2 h 1.690 g (10 mmol) **12** containing *ca* 20% **13** and the viscous system was stirred at 25°C for 4 days. TLC (MeOH/conc. NH_3 4:1 v/v) showed the product, **6**, R_f 0.52, **16** R_f 0.78 and **13** R_f 0.91. Extraction with Et_2O (5 × 10 ml) and $CHCl_3$ (5 × 5 ml) gave 804 mg organics, mainly **13**, (TLC, Et_2O, **13** R_f 0.42, **12** R_f 0.16 and **16** R_f 0.08). The aqueous phase was acidified to pH 1.5 with 1:1 HCl, stirred at 25°C for 3 h and centrifuged. The white solid was washed with cold H_2O (2 × 1.5 ml) and dried (weight 348 mg containing 211 mg As_2O_3). The washings and the supernatant were evaporated and dried to give 1.655 g off-white solid which was extracted with ~99% ethanol (7 × 3 ml) at 25°C. The residue (872 mg) contained 78 mg As_2O_3. The ethanolic solution was evaporated and dried in vacuo to give 684 mg off-white solid containing the product **6** (calculated yields: 34% on the As(III) or 17% on **12** used), 5.4% As_2O_3, about 5% **16**, and NaBr. To 684 mg of the solid (containing a calculated 1.7 mmol of **6**) was added absolute ethanol (9 ml), warmed to 60°C and to the heterogeneous (NaBr) system 0.71 ml (6.8 mmol) thiophenol was added. The system was stirred for 90 min at 25°C. TLC (MeOH/conc. NH_3 4:1) showed complete reaction of **6**. Centrifugation gave a solid (238 mg which was a mixture of NaBr and most of the As_2O_3) which was washed with $CHCl_3$ (2 × 2 ml). The washings and the supernatant were evaporated and dried in vacuo to give 987 mg of a solid. From the solid most of the diphenyldisulfide was extracted by *n*-pentane (3 × 3 ml) and the product, **17**, [containing traces of **16** and very small amounts of PhSSPh and $As(SPh)_3$] was extracted with $CHCl_3$ (3 × 3 ml). The chloroform extracts were washed with H_2O (3 × 3 ml) to remove 48 mg of **16**, evaporated and dried in vacuo to give 493 mg of slightly impure product **17** as a gum. Yields: 26% on As(III) or 13% on **12**. Calculated for $C_{16}H_{19}AsO_2S_2$: 19.59% As, found 18.53%. IR (film, main bands; see also Reference 6): 3422 broad, s, 3052 s, 1578 s, 1476 s, 1436 s, 1066 s, 1022 s, 746 s, 690 s. ^{1}H-NMR ($CDCl_3$) δ: 1.6 (m, C$\underline{H}_2$), 2.2 (m, C$\underline{H}_2$As), 3.6 (m, C$\underline{H}_2$OH), 4.3 (m, C$\underline{H}$OH), 7.3 (m, C$_6\underline{H}_5$).

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REFERENCES

1. R. Engel, *Chem. Rev.*, **77,** 349 (1977).
2. C. Pratt, Y.-J. Liu, T.-Y. Chu, K. Melkonian, B. E. Tropp and R. Engel, *Can. J. Chem.*, **70,** 2135 (1992).
3. J. W. Long and W. J. Ray, Jr., *Biochemistry*, **12,** 3932 (1973).
4. G. M. Tsivgoulis, D. N. Sotiropoulos and P. V. Ioannou, *Phosphorus, Sulfur, and Silicon*, **63,** 329 (1991).
5. S. V. Serves, G. M. Tsivgoulis, D. N. Sotiropoulos and P. V. Ioannou, *Phosphorus, Sulfur, and Silicon*, **71,** 99 (1992).
6. S. V. Serves, D. N. Sotiropoulos, P. V. Ioannou and M. K. Jain, *Phosphorus, Sulfur, and Silicon*, **81,** 181 (1993).
7. G. M. Tsivgoulis, D. N. Sotiropoulos and P. V. Ioannou, *Phosphorus, Sulfur, and Silicon*, **57,** 189 (1991).
8. G. Meyer, *Ber. Dtsch. Chem. Ges.*, **16,** 1439 (1883).
9. S. V. Serves, D. N. Sotiropoulos, P. V. Ioannou and H. B. F. Dixon, *Phosphorus, Sulfur and Silicon*, in print (1994).
10. C. K. Banks, J. F. Morgan, R. L. Clark, E. B. Hatlelid, F. H. Kahler, H. W. Paxton, E. J. Cragoe, R. J. Andres, B. Elpern, R. F. Coles, J. Lawhead and C. S. Hamilton, *J. Am. Chem. Soc.*, **69,** 927 (1947).
11. R. Pietsch, *Monatsch. Chem.*, **96,** 138 (1965).
12. C. F. McBrearty, Jr., K. Irgolic and R. A. Zingaro, *J. Organometal. Chem.*, **12,** 377 (1968).
13. K.-C. Tang, B. E. Tropp and R. Engel, *Tetrahedron*, **34,** 2873 (1978).
14. R. H. Mazur, W. N. White, D. A. Semenov, C. C. Lee, M. S. Silver and J. D. Roberts, *J. Am. Chem. Soc.*, **81,** 4390 (1959).
15. J.-C. Tang, B. E. Tropp, R. Engel and A. F. Rosenthal, *Chem. Phys. Lipids*, **17,** 169 (1976).
16. H. W. Heine, A. D. Miller, W. H. Barton and R. W. Greiner, *J. Am. Chem. Soc.*, **75,** 4778 (1953).
17. T. M. Loehr and R. A. Plane, *Inorg. Chem.*, **7,** 1708 (1968).

18. H.-J. Bielig, G. Lützel and A. Reidies, *Ber.*, **89,** 775 (1956).
19. N. A. Chadaeva, G. K. Kamai and G. M. Usacheva, *J. Gen. Chem. U.S.S.R.*, **36,** 718 (1966).
20. R. P. Ambler, *Biochem. J.*, **89,** 349 (1963).
21. A. I. Vogel, "Textbook of Quantitative Inorganic Analysis," (Longman, London, 1979), a) p. 378, b) p. 498.
22. W. W. Scott and N. H. Furman, "Standard Methods of Chemical Analysis," (van Nostrand, London, 1939) 5th ed., pp. 67, 115.
23. H. E. Wade and D. M. Morgan, *Nature*, **171,** 529 (1953).