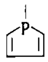
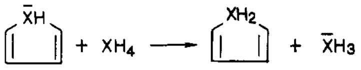


Figure 3. The phosphole nucleus.

In order to quantitatively assess the extent of electron delocalization in the ground state of 1 and to compare it to the cyclopentadienyl anion, we calculated energy differences for the isodesmic[9] reaction shown in eq 1 (X = C or Si). The energy difference of 73.4 kcal/mol obtained



(1)

for this reaction when X = C[10] provides an estimate of the resonance energy for the cyclopentadienyl anion. This value is in reasonable agreement with the resonance energy estimate obtained by Gordon et al.[2] at the 3-21G//STO-2G level of sophistication. For X = Si, the C_s conformation provides an energy difference of only 2.2 kcal/mol.[12] This value is substantially smaller than the previous estimate[2] of the resonance energy of 1 (23 kcal/mol) which was based on the C_{2v}, planar structure. Since pyramidalization at silicon should decrease the efficiency of silicon–carbon (p–p) π overlap[13] and hence the extent of electron delocalization, these findings are in complete accord with our qualitative expectations. The present calculations thus substantially lower the current estimate of the resonance energy for 1. On the basis of these calculations we conclude that the ground state of 1 has only ca. 3% of the resonance stabilization exhibited by its carbon analogue, the cyclopentadienyl anion.

An interesting comparison may be made between 1 and the isoelectronic phospholes (Figure 3). The barrier to pyramidal inversion in phosphine is calculated to be at least 37 kcal/mol.[14] In simple phospholes the barrier to pyramidal inversion at phosphorus is substantially decreased from this value to ca. 16 kcal/mol.[15] Structurally, however, the pyramidality at phosphorus is not significantly altered in these compounds relative to that found for phosphine.[16] Similarly, we find that the inversion barrier in 1 (16.2 kcal/mol) is significantly reduced relative to the ca. 26 kcal/mol obtained[17] for the silyl anion. Further, using the sum of the angles about silicon as a measure of pyramidality, the C_s conformation (290.5°) does not differ significantly from the silyl anion itself (291.1°,[17] 292.8° [18]). Evidently, as for the phosphines,[15,16] substituents that lower the barrier to pyramidal inversion at silicon in the silyl anions do not necessarily cause a flattening of the silicon pyramid.[19]

The inversion barrier and resonance energy calculated in the present work lead to a number of interesting predictions regarding the static and dynamic stereochemistry of 1 and its closely related derivatives. For example, while attempts to measure the inversion barrier in a silyl anion[20] have long been thwarted by barriers that exceed the limits of dynamic NMR (DNMR) methods (i.e., >24 kcal/mol),[20] the present calculations suggest that investigations of suitable derivatives of 1 would be a promising direction for future experimental efforts in this area. In addition, the current level of interest in generating η^5 metal complexes of derivatives of 1[21] calls for detailed understanding of the electronic structure of the silacyclopentadienyl anion fragment.[2] On the basis of our relatively localized picture of electron distribution in the π system of 1, one would predict that the stability of these η^5 metal complexes will be significantly lower than that found for their all-carbon analogues.

Acknowledgment is made to IBM Corporation and to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research. Thanks go to Prof. M. Gordon for helpful discussions.

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(10) All structures were completely optimized for parent symmetries. Total energies in hartrees/molecule (6-31G*) are: C_5H_6, −192.79172 (C_{2v}), C–H(CH_2) = 1.089 Å, C_α–H = 1.073 Å, C_β–H = 1.074 Å, CH_2–C_α = 1.506 Å, C_α–C_β = 1.328 Å, C_β–C_β = 1.477 Å, C_α–CH_2–C_α = 102.5°, CH_2–C_α–C_β = 109.6°, C_α–C_β–C_β = 109.2°, CH_2–C_α–H = 123.7°, H–C–H = 106.7°, C_α–C_β–H = 126.4°, C_α–CH_2–H = 111.9°; CH_3^-, −39.46684 (C_{3v}, obtained from CMU data base[4]). $C_5H_5^-$, −192.180412 (D_{5h}) C–H = 1.080 Å, C–C = 1.402 Å; CH_4, −40.19517 (T_d, obtained from CMU data base[4]). Experimentally the resonance energy for the cyclopentadienyl anion is estimated at 24–27 kcal/mol.[11] This suggests that any systematic error in our calculations will lead to an overestimation of the resonance energies.

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Correlation of the Rates of Solvolysis of the Methyldiphenylsulfonium Ion[1]

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In conjunction with the development[2,3] (eq 1) of a scale of solvent nucleophilicities ($N_{Et_3O^+}$) based upon the specific rates of solvolysis of the triethyloxonium ion in a given solvent (k) and in the standard (80% ethanol) solvent (k_0),

$$\log (k/k_0) = N_{Et_3O^+} \qquad (1)$$

we tested the utility of the scale in the correlation of the rates of solvolysis of other RX^+ substrates. A measure of the sensitivity (l) of the specific rates of solvolysis of RX^+ substrates towards changes in solvent nucleophilicity can be obtained from eq 2.

$$\log (k/k_0)_{RX^+} = lN_{Et_3O^+} \qquad (2)$$

Obvious candidates for study are the structurally related trisubstituted sulfonium ions. These react, however, much

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Table I. Specific Rates of Solvolysis of the Methyldiphenylsulfonium Ion[a,b]

solvent	temp, °C	10^8k, s^{-1}	solvent	temp, °C	10^8k, s^{-1}
H_2O	50.0	3.99 ± 0.22[c]	AcOH	90.4	167 ± 10[d]
H_2O	70.6	47.8 ± 2.1	EtOH	40.4	42.7 ± 1.4
H_2O	80.4	129 ± 3	EtOH	50.0	145 ± 3
H_2O	90.4	406 ± 31[d]	EtOH	50.6	158 ± 2
AcOH	70.6	19.1 ± 0.6[c]	EtOH	60.5	466 ± 19
AcOH	80.4	54.2 ± 3.2	EtOH	70.4	1279 ± 58

[a] Specific rates (and standard deviations) determined from duplicate runs, using a ca. 0.006 M solution of the trifluoromethanesulfonate salt. [b] Values for the enthalpies (kcal mol^{-1}) and entropies (eu) of activation, with associated standard errors, are 25.8 ± 0.1 and −12.6 ± 0.3 for H_2O, 26.5 ± 0.9 and −12.4 ± 2.6 for AcOH, and 23.5 ± 0.4 and −12.9 ± 1.3 for EtOH. [c] Single determination. [d] Using sealed ampules.

Table II. Specific Rates of Solvolysis of the Methyldiphenylsulfonium Ion[a] in Aqueous–Organic Solvents at 50.0 °C

solvent[b]	10^8k, s^{-1}	$\log (k/k_0)$[c]	solvent[b]	10^8k, s^{-1}	$\log (k/k^0)$[c]
100% EtOH	*d*	+0.36	95% acetone	21.1 ± 1.1	−0.48
80% EtOH	63.8 ± 1.3[e]	0.00	90% acetone	30.7 ± 1.2	−0.32
60% EtOH	29.5 ± 1.1[e]	−0.33	80% acetone	32.7 ± 1.2	−0.29
40% EtOH	12.8 ± 0.8[e]	−0.70	60% acetone	23.8 ± 1.1	−0.43
20% EtOH	6.48 ± 0.30	−0.99	40% acetone	12.7 ± 0.6	−0.70
100% H_2O	*d*	−1.20	80% dioxane	60.3 ± 2.6	−0.02
100% MeOH	106 ± 2	+0.22	70% dioxane	36.4 ± 1.7	−0.24
80% MeOH	53.0 ± 2.9	−0.08	60% dioxane	34.1 ± 1.4	−0.27
60% MeOH	23.2 ± 1.0	−0.44	50% TFE[f,g]	1.90 ± 0.14	−1.53
40% MeOH	11.7 ± 0.3	−0.74	100% AcOH	1.48 ± 0.18[h]	−1.63
20% MeOH	5.50 ± 0.28	−1.06			

[a] See footnote *a* of Table I. [b] On a volume–volume basis at 25.0 °C, with the other component water. [c] k_0 is the specific rate in the standard solvent (80% EtOH). [d] Value is in Table I. [e] Adjusted from a value determined at 50.6 °C by multiplying by 0.918 (the ratio of the specific rates at 50.0 and 50.6 °C for ethanolysis) [f] On a weight–weight basis. [g] In 90% TFE (w/w) an approximate specific rate of 0.34 (±0.04) × 10^{-8} s^{-1} was obtained. [h] Obtained by extrapolation, using the Arrhenius equation, of data reported in Table I.

slower than the corresponding oxonium ions. In 90% acetone at 100 °C, less than 1% solvolysis of the trimethylsulfonium ion was observed after 3 days.[4] Specific rates at 100 °C of 24 × 10^{-8} s^{-1} for methanolysis, 16 × 10^{-8} s^{-1} for ethanolysis and 0.13 × 10^{-8} s^{-1} for hydrolysis have been reported;[5] the value in water corresponds to 1% hydrolysis after 90 days. In another study[6] at 100 °C, the specific rate of ethanolysis was reproduced but a higher value of 0.81 × 10^{-8} s^{-1} (from extrapolation of data obtained at higher temperatures) was claimed for hydrolysis.

Since we included measurements in solvents with nucleophilicities considerably below that of water, which was already of extremely low reactivity, an increased leaving group ability within the substrate was clearly necessary. One way in which the susceptibility of a sulfonium ion to nucleophilic attack can be increased is by a partial replacement of methyl groups by phenyl groups. For example, Coward and Sweet[7] found that, for reaction with pyrrolidine or *n*-butylamine in acetonitrile at 25 °C, the methyldiphenylsulfonium ion reacted 20 times faster than the dimethylphenylsulfonium ion.

As one would expect, the increased nucleofugality of aryl sulfides relative to alkyl sulfides is reflected in a reduced nucleophilicity toward alkyl halides.[8] However, in synthetic procedures, the reduced nucleophilicity can be counteracted by the use of silver ion assistance.[9]

We have prepared (eq 3) methyldiphenylsulfonium trifluoromethanesulfonate (triflate) and have studied the kinetics of the solvolysis in a variety of pure and aqueous–organic solvents (eq 4). The influence of a *p*-nitro substituent also has been investigated.

$$\mathrm{Ph_2S + MeI + AgOTf \xrightarrow{CHCl_3} MeSPh_2{}^+OTf^- + AgI\downarrow} \qquad (3)$$

$$\mathrm{MeSPh_2{}^+ + 2SOH \rightarrow MeOS + SPh_2 + SOH_2{}^+} \qquad (4)$$

Results

Solvolyses in Water, Acetic Acid, and Ethanol. Rates of solvolysis were determined at three or more temperatures in the 40–90 °C range. Constant integrated first-order rate coefficients were obtained throughout each run. All of the individual integrated values, usually for duplicate runs, were averaged. These averages are reported, together with the activation parameters (at 343.8 K) obtained from a treatment of the data in terms of the Eyring equation, within Table I.

Solvolyses in Solvents of Varying Nucleophilicity. A study was made, at 50.0 °C, in methanol and in mixtures of water with ethanol, methanol, acetone, dioxane, or 2,2,2-trifluoroethanol (TFE). All runs were performed, at least, in duplicate, and average values for the specific rates are reported within Table II, together with the logarithms of the ratio of the specific rate in a given solvent relative to that in 80% ethanol.

Ethanolysis of Methyl(*p*-nitrophenyl)phenylsulfonium Trifluoromethanesulfonate. The kinetics of this reaction were studied, with duplicate determinations, in the 40–70 °C range. Average specific rates of 7.17 (±0.12) × 10^{-6} s^{-1} at 40.6 °C, 20.4 (± 0.7) × 10^{-6} s^{-1} at 50.0 °C, 62.9 (±1.3) × 10^{-6} s^{-1} at 60.1 °C, and 176 (±13) × 10^{-6} s^{-1} at 70.4 °C were obtained. The derived activation parameters (Eyring equation at 343.6 K) were 22.4 ± 0.2 kcal mol^{-1} for the enthalpy of activation and −10.8 ± 0.7 eu for the entropy of activation.

Discussion

Although the methyldiphenylsulfonium ion is of higher solvolytic reactivity than the trimethylsulfonium ion,[4-6] specific rates at 50.0 °C could be obtained directly within a reasonable period of time only for solvents with nucleophilicity values ($N_{Et_3O^+}$) of above about −1. This se-

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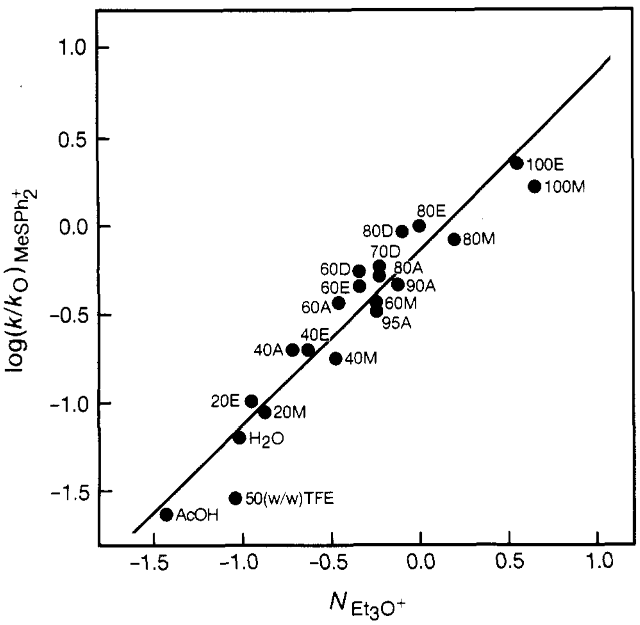

Figure 1. Plot of the logarithms of the relative specific rates of solvolysis of the methyldiphenylsulfonium ion, at 50.0 °C, against $N_{Et_3O^+}$ values. For aqueous–organic mixtures, the number represents the percentage (by volume) of the organic component and E, M, A, and D represent ethanol, methanol, acetone, and dioxane, respectively.

verely restricted the range for which eq 2 could be conveniently tested. However, data of reasonable precision (Table II) were obtained for 21 solvents for which $N_{Et_3O^+}$ values were available.[2,3] The correlation is shown in Figure 1. A satisfactory correlation is obtained with only the point for 50% TFE showing appreciable deviation. From the data for the 21 solvents, the slope (l value) was calculated as 0.988 ± 0.069 (standard error) and the intercept was calculated as -0.137 ± 0.044; the correlation coefficient was 0.957. Inspection of Figure 1 shows that if the binary systems were individually correlated, there would be marked dispersions; dispersion is especially noticeable when the specific rates of solvolysis in aqueous methanol and aqueous ethanol are compared.

If other factors had been identical, one would have expected an l value of greater than unity since methyl derivatives have been found to be more sensitive to changes in solvent nucleophilicity than ethyl derivatives.[2,10] However, the $N_{Et_3O^+}$ scale was established from studies carried out at a 50 °C lower temperature than the present study, and it has frequently been demonstrated that sensitivity parameters such as l, m (solvent ionizing power), or the Hammett ρ usually fall in value with increasing temperature.[11]

Introduction of phenyl groups, while favorably increasing the rates of solvolysis, could complicate the interpretation of the influence of solvent variation. The energetics of any specific interactions between the solvent and the electron-rich aromatic rings would differ for the initial and transition states, and, further, this differential would vary with solvent composition. Possibly, some of the modest scatter observed in the plot against $N_{Et_3O^+}$, a scale based on a standard substrate not containing aromatic rings, can be ascribed to an effect of this nature. Bunton, Mhala, and Moffatt[12] have proposed that such effects could be important in the dispersion observed in plots of the logarithms of the specific rates of solvolysis of diphenylmethyl chloride against Y values.

The acceptable correlation with an appreciable l value illustrates the utility of the $N_{Et_3O^+}$ scale, and it strongly supports the previously expressed view that solvolyses[5,6] and other nucleophilic substitution reactions[4-7,13] at the methyl carbon of a $MeSR_2^+$ substrate are S_N2 in character.

The negative entropies of activation observed for hydrolysis, acetolysis, and ethanolysis (Table I) also support an S_N2 mechanism for the solvolyses. The values, within the range of −12.4 to −12.9 eu, are much lower than values of +15.7 to +20.3 eu observed for identical solvolyses of the 1-adamantyldimethylsulfonium ion.[3] Positive values, within this range, have also been observed for solvolyses of the *tert*-butyldimethylsulfonium[14,15] and (α-phenylethyl)dimethylsulfonium[14] ions. While a degree of caution must be exercised in any mechanistic interpretation of $\Delta S^\ddagger$ values, the sharp distinction between the negative values for substrates for which one would predict S_N2 reaction and the positive values for substrates for which one would predict S_N1 reaction is unusually striking. The ratios of specific rates in ethanol and water of 36 at 50 °C and 27 at 70 °C (using data from Table I) appear to be more consistent with a ratio for corresponding trimethylsulfonium ion solvolyses at 100 °C of 22[6] rather than 123.[5]

The extrapolated specific rate of ethanolysis at 100 °C, using the Arrhenius equation, is 2.18×10^{-4} s^{-1}. In conjunction with a mean value for the specific rate for ethanolysis of the trimethylsulfonium ion at this temperature (16.9×10^{-8} s^{-1}),[5,6] and allowing for the three equivalent positions in Me_3S^+ for attack, one can estimate that, for this system, diphenyl sulfide is 3900 times more nucleofugal than dimethyl sulfide. A previous attempt to increase further the leaving group ability by introduction of two p-nitro substituents failed.[7] Use of bis(p-nitrophenyl) sulfide instead of diphenyl sulfide in reaction with methyl iodide and silver perchlorate led to recovery of unreacted sulfide, which was assumed to be of too low nucleophilicity. The p-nitrophenyl phenyl sulfide is intermediate in character, and it was found to react with methyl iodide and silver trifluoromethanesulfonate in nitromethane to give the sulfonium salt. Ethanolysis of the methyl (p-nitrophenyl)phenylsulfonium ion was faster than the parent (unsubstituted) ion by a factor of 14, at both 50.0 and 70.4 °C. A Hammett ρ value was calculated based upon the p-nitro derivative and the unsubstituted compound. A modified σ value of 0.716, estimated from a study of the ethanolyses of adamantyl arenesulfonates,[16] was used. This value takes into account the solvent dependence[17] of the σ values for a nitro substituent. Values of 1.60 at 50.0 °C and 1.59 at 70.4 °C were obtained. These values are in remarkably good agreement with values of 1.60 obtained[7] for reactions of aryldimethylsulfonium ions with hydroxide ion in water at 78.5 °C and 1.74 obtained[7] for reactions of aryldimethylsulfonium ions with either pyrrolidine or n-butylamine in acetonitrile at 25.0 °C.

Experimental Section

Materials. The purifications of acetone, dioxane, ethanol, and methanol were as previously described.[18] The purifications of

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acetic acid,[19] 2,2,2-trifluoroethanol,[20] iodomethane,[21] chloroform,[22] and nitromethane[22] were also carried out by previously described procedures. Diphenyl sulfide (Aldrich), *p*-nitrophenyl phenyl sulfide (Aldrich), and silver trifluoromethanesulfonate (Aldrich) were used without further purification.

Methyldiphenylsulfonium Trifluoromethanesulfonate. Methyl iodide (2.03 g, 14.3 mmol) was added to a solution of diphenyl sulfide (2.83 g, 15.2 mmol) and silver trifluoromethanesulfonate (3.67 g, 14.3 mmol) in 15 mL of chloroform. A rapid mildly exothermic reaction occurred, and after filtration through Celite, concentration of the filtrate (rotary evaporator) gave a yellow-green viscous liquid. Addition of pentane and cooling in an ice-salt bath converted the liquid to a pale olive paste. Filtration and rinsing of the paste with ether led to a fine off-white powder: 3.44 g (68.7%); mp 94-97.5 °C; IR (KBr disk) 3090, 3070, 3020, 1475, 1445, 1260, 1170, 1150, 1020, 990, 755, 740, 685 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.68 (s, CH_3, 3 H), 7.50-8.07 (m, C_6H_5, 10 H). Anal. Calcd for $C_{14}H_{13}F_3O_3S_2$: C, 48.00; H, 3.74; S, 18.30. Found: C, 47.90; H, 3.86; S, 18.55. Complete ethanolysis of a tared sample, in a sealed tube at 65 °C for 720 h, led to a titration against a standardized solution of NaOMe in MeOH corresponding to 101.5% of the theoretical value.

Methyl(*p*-nitrophenyl)phenylsulfonium Trifluoromethanesulfonate. Silver trifluoromethanesulfonate (3.67 g, 14.3 mmol) dissolved in 50 mL of nitromethane was added to a mixture of *p*-nitrophenyl phenyl sulfide (3.52 g, 15.2 mmol), methyl iodide (2.03 g, 14.3 mmol), and nitromethane (5 mL). An immediate precipitate of silver iodide was observed. After the mixture was stirred for 1.5 h, acetonitrile (50 mL) was added and stirring was continued for 15 min. Filtration and concentration of the filtrate led to a yellow-green oil that slowly crystallized at 0 °C. Washing with ether led to a colorless powder: 3.33 g (58.9%); mp 131.5-133 °C; IR (KBr disk) 3060, 3020, 2930, 1600, 1520, 1425, 1345, 1285, 1235, 1140, 1025, 760, 735, 680, 670 cm^{-1}; ^{1}H NMR (CD_3CN) δ 3.67 (s, CH_3, 3 H), 7.22-8.56 (m, aromatic, 9 H). Anal. Calcd for $C_{14}H_{12}NF_3O_5S_2$: C, 42.53; H, 3.06; N, 3.54; S, 16.22. Found: C, 42.61; H, 3.22; N, 3.55; S, 16.06. Complete ethanolysis of a tared sample, in a sealed tube at 65 °C for 670 h, led to a titration against a standardized solution of NaOMe in MeOH corresponding to 101.1% of the theoretical value.

Kinetic Procedures. Each run was carried out by the removal at appropriate time intervals of 5-mL portions from 50 mL of a solution initially ca.6 × 10^{-3} M in reactant. At 50 °C and below, the runs were slow and the interval before determination of the infinity titer was reduced by heating a sample of volume slightly in excess of 5 mL in a sealed ampule at 65 °C. After completion of the solvolysis, the sample was returned to the temperature of the run prior to removal of a 5-mL portion for titration.

For experiments in water, alcohols, and aqueous-organic mixtures, the 5-mL portions were titrated in 25 mL of cooled acetone (ice bath), containing Lacmoid (resorcinol blue) as indicator, against a standardized solution of NaOMe in MeOH. The titration procedures for runs in acetic acid and the calculation of the first-order solvolytic rate coefficients were as previously described.[2]

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Registry No. Methyldiphenylsulfonium trifluoromethanesulfonate, 105229-70-7; methyl(*p*-nitrophenyl)phenylsulfonium trifluoromethanesulfonate, 105229-72-9.

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A Systematic Degradation of Zincophorin: A Stereoselective Synthesis of the C_{17}-C_{25} Fragment

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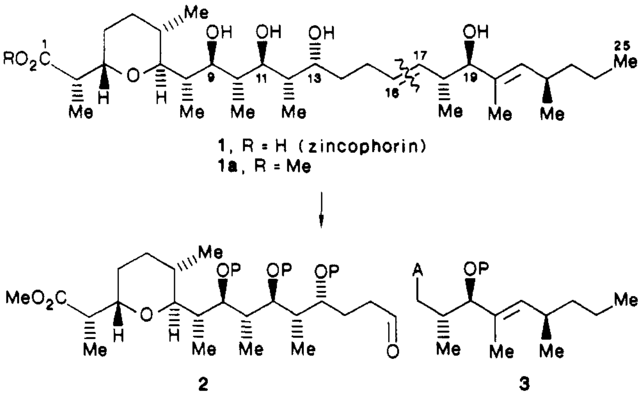
Zincophorin (M144255)(1),[1] recently isolated from a strain of *Streptomyces griseus.*, has a remarkable specificity for divalent cations, particularly zinc. It shows good in vitro activity against Gram-positive bacteria. The combination of ionophoric and biological behavior of zincophorin renders it an attractive system for chemical investigation. Access to structurally modified congeners might clarify the roles of various substructural units on binding and on antibiotic properties.



1, R = H (zincophorin)
1a, R = Me

2

3

This goal of synthesizing analogues would be well served by a degradation of zincophorin in a fashion wherein the components of the cleavage can be retrieved. In this paper, we report the attainment of this goal. The method described here has the added feature that the degradation products can be modified and processed with a view toward eventual recombination (cf. systems 2 and 3: P = protecting groups; A promotes nucleophilic character at C_{17}).

The key reaction is the highly selective osmylation[2] of zincophorin methyl ester (**1a**).[1] Treatment of **1a** with OsO_4 (0.1 equiv)[3] and NMO (3 equiv) in aqueous THF followed by periodate cleavage [$NaIO_4$, 4% AcOH/MeOH/THF (1:1:2)] of the resulting 1,2-diol provided compounds **4** (76%)[4,5] and aldehyde **5** (57%) (Scheme I). Oxidation [10 equiv of Ag_2CO_3/Celite, PhH, Δ][6] of the lactol mixture **4** afforded the stable γ-lactone **6** in 96% yield, *thus accomplishing differentiation between the hydroxyl group at* C_{13} *from those at* C_9 *and* C_{11}. Protection of the latter hydroxyl groups as their acetonide [*p*-TsOH, anhydrous $CuSO_4$, acetone] was achieved, leading to compound **7** (96%). Selective reduction of the γ-lactone to the C_{13},C_{16}-diol *in the presence of the methyl ester*[7] proceeded

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[1] Books, H. A.; Garoner, D.; Poyser, J. P.; King, T. J. *J. Antibiot.* **1984**, *37*, 1501.

[2] The C_{16}-C_{17} double bond of zincophorin free acid has also been selectively hydrogenated, see ref 1.

[3] VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.

[4] Compound 4 exists as a 2:1 mixture of lactols and open chain aldehyde. The intermediate is unstable due to formation of an anhydro sugar upon standing.

[5] All new compounds reported herein gave ^{1}H NMR, IR, optical rotation, and MS or combustion analytical data consistent with the assigned structure.

[6] Fetizon, M.; Golfier, M. *C. R. Seances Acad. Sci., Ser. C* **1968**, *267*, 900.

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