9.15; N, 11.56. Found: C, 59.15; H, 9.20; N, 11.29.

Benzylacetamide (2f). Under a nitrogen atmosphere in a 50-mL round-bottom flask equipped with a magnetic stir bar and a rubber septum was placed 570 mg (4.3 mmol) of benzyl azide. To the system was added 1.2 mL (1.3 g, 17.2 mmol) of thioacetic acid. This solution was stirred at room temperature for 1 h, and the thioacetic acid was removed with a rotary evaporator. The resulting oil was subjected to flash column chromatography (50 g of silica gel) using 1:1 ether/pentane followed by ether as the eluant to obtain 580 mg (91% yield) of benzylacetamide as a white crystalline solid, mp 58–60 °C.

Reaction of Benzylamine with Thioacetic Acid. Under a nitrogen atmosphere in a 50-mL round-bottom flask equipped with a magnetic stir bar and a rubber septum was placed 0.54 mL (535 mg, 5 mmol) of benzylamine. To the system was added 1.4 mL (1.5 g, 20 mmol) of thioacetic acid, upon which a precipitate formed instantaneously. The thioacetic acid was removed with a rotary evaporator to obtain 740 mg (quantitative yield) of benzylacetamide as a yellow solid. Recrystallization from hexanes afforded 690 mg (92% yield) of pure benzylacetamide. The physical and spectral properties of the material obtained in this manner were identical with those of the product obtained upon treatment of benzylazide with thioacetic acid.

(2*R*,4*S*)-4-Acetamido-1-benzyl-2-carbomethoxypyrrolidine (2c): mp 62–64 °C; ^{1}H NMR δ 1.92 (s, 3 H), 1.96 (dd, 1 H, J = 2.6, 7.7), 2.4 (m, 2 H), 3.35 (dd, 1 H, J = 6.6, 9.6), 3.56 (dd, 1 H, J = 5.7, 8.6), 3.67 (d, 1 H, J = 12.9), 3.69 (s, 3 H), 3.86 (d, 1 H, J = 13.2), 4.51 (br, d, NH, J = 6.6), 5.51 (m, 1 H), 7.27 (m, 5 H); mass spectrum, m/z 277 (parent + H). Anal. Calcd for $C_{15}H_{20}N_2O_3 \cdot {}^2/_3H_2O$: C, 62.47; H, 7.45; N, 9.71. Found: C, 62.60; H, 7.27; N, 9.71.

(2*S*,4*R*)-2-(Acetamidomethyl)-1-(*tert*-butoxycarbonyl)-4-[(methylsulfonyl)oxy]pyrrolidine (2h): ^{1}H NMR δ 1.49 (s, 9 H), 1.99 (s, 3 H), 2.42 (ddt, 1 H, J = 2.3, 7.5, 14.3), 3.04 (s, 3 H), 3.20 (br, 1 H), 3.55 (br, 2 H), 3.91 (br, d, 1 H, J = 13.2), 4.10 (d, 1 H, J = 7.0), 4.14 (d, 1 H, J = 7.0), 5.16 (m, 1 H), 5.90 (br, NH); mass spectrum, m/z 337 (parent + H), 298, 281, 237. Anal. Calcd for $C_{13}H_{24}N_2O_6S \cdot {}^2/_3H_2O$: C, 44.83; H, 7.27; N, 8.04. Found: C, 45.01; H, 7.20; N, 7.64.

Registry No. **1a**, 113451-51-7; **1b**, 113451-52-8; **1c**, 113451-53-9; **1d**, 44961-22-0; **1e**, 19573-22-9; **1f**, 622-79-7; **1g**, 57294-86-7; **1h**, 113451-54-0; **2a**, 113451-55-1; **2b**, 113451-56-2; **2c**, 113451-57-3; **2d**, 14202-55-2; **2e**, 1124-46-5; **2f**, 588-46-5; **2g**, 6158-94-7; **2h**, 113451-58-4; **3**, 113451-59-5; HSAc, 507-09-5; $PhCH_2NH_2$, 100-46-9.

Thioaldehyde Anion Radicals

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Whereas the radical anions of aldehydes have long been known and extensively investigated by ESR spectroscopy,[1,2] the radical anions of the corresponding thioaldehydes had not been directly detected. On the other hand, a large amount of information is available on the radical anions of thioketones,[3-8] allowing the comparison of their spectral properties with those of the corresponding ketyl radicals. The absence of examples of thioaldehyde radical anions is due to the fact that the parent molecules, contrary to thioketones, are too unstable to be isolated.[9] As a consequence, the reactions employed to produce the radical anions from thioketones could not be applied to thioaldehydes.

It is known, however, that the benzaldehyde radical anion **1** can be obtained by radiolysis of benzyl alcohol in aqueous alkaline solutions.[10] We observed that the same

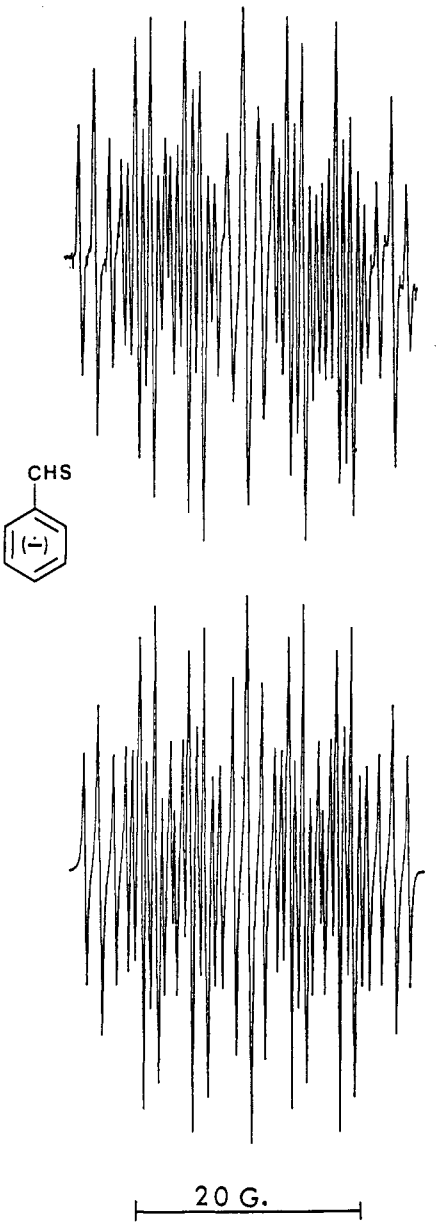

Figure 1. Experimental ESR spectrum (upper trace) of $PhCH{=}S^{\bullet-}$ (**2**) obtained by photolysis of $PhCH_2SH$ in EtOK/EtOH at room temperature. The computer simulation (lower trace) has been obtained with the a_H values listed in Table I and a line width of 0.2 G. To match the experimental intensities, the a_H splittings of H-3 and H-5 must differ by about 0.15 G.

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Table I. Hyperfine Splitting Constants (a_H in Gauss) and g Factors for the Radical Anion 1[a] and for the Radical Anions 2-4[b]

compd	H-2	H-3	H-4	H-5	H-6	HC=X	g factor
PhCHO$^{\bullet-}$, (1)	4.87	1.55	6.12	1.20	4.0	12.1	2.0033
PhCHS$^{\bullet-}$, (2)	4.30	1.39	5.0	1.23	3.68	13.1	2.0058
3		1.50		1.50		15.6	2.0057
3a		1.50		1.50		2.4	2.0057
3b						15.6	2.0057
4		2.1		2.1		10.3	2.0034

[a] Obtained by photolysis either of benzyl alcohol or of benzaldehyde. [b] In EtOK/EtOH at room temperature. X is oxygen in 1 and 4 and sulfur in 2, 3, 3a, and 3b.

radical can be also obtained by UV photolysis of benzyl alcohol in EtOK/EtOH. The ESR parameters are equal to those obtained by reacting benzaldehyde under the same conditions. It has been also reported that the reaction of benzyl mercaptan with a strong base (*n*-butyllithium) afforded the dianion of thiobenzaldehyde.[11]

It was thus conceivable to expect that the radical anion of thiobenzaldehyde (PhCH=S$^{\bullet-}$,2) could be obtained by photolysis of benzyl mercaptan ($PhCH_2SH$) in an alkaline medium. In fact, the ESR spectrum reported in Figure 1 represents unambiguous evidence of the existence of radical 2 in solution. The parameters employed for the computer simulation of the ESR spectrum are listed in Table I.

An additional proof of the nature of radical 2 is offered by the photolysis, in the same alkaline medium, of the only available aromatic thioaldehyde, 2,4,6-tri-*tert*-butylthiobenzaldehyde,[12] stable enough to be isolated. The ESR spectrum of the resulting radical anion 3 has, in fact, a g value (Table I) equal to that of 2 (2.0058), typical[7] for radicals having an unpaired electron interacting with a sulfur atom. The g factors of 2 and 3 are, accordingly, much higher than those of the anions derived from the corresponding aldehydes (4 and 1). Substitution of the HCS hydrogen with deuterium in 2,4,6-tri-*tert*-butylthiobenzaldehyde yields a radical (3a) whose ESR spectrum displays an a_D splitting (1:1:1 triplet) equal to 2.4 G (Table I). This value, 6.5 times smaller than the corresponding a_H splitting (doublet) of the thioaldehydic hydrogen in 3, is that expected on the basis of the H/D gyromagnetic ratio. Deuterium labeling of the 3- and 5-positions of the benzene ring yields an anion radical (3b) where the splittings of the corresponding hydrogens have disappeared (the a_D splittings are in this case too small to be detected).

Inspection of the a_H values of 2 shows that those corresponding to the pair of ortho hydrogens (positions 2, 6) as well as to the pair of meta hydrogens (positions 3, 5) are not equivalent. This indicates that the radical adopts a planar (or quasi-planar) conformation with a substantial barrier to the Ar–CHS rotation. This feature is the same reported[1] for radical 1, and accordingly, the assignment of the a_H values in 2 has been made by analogy.

In contrast, the splittings for the pairs of the meta hydrogens in 3 and 4 are equal. This suggests that, owing to the hindrance of the two ortho *tert*-butyl groups, the HC=X plane (X being O or S) is either perpendicular to the aromatic ring or twisted by an angle sufficiently close to 90° as to make the passage through the perpendicular transition state much faster than in the case of 1 and 2. This fast motion would thus create a dynamic plane of symmetry leading, in practice, to the same symmetry expected for a perpendicular conformer. Support for this interpretation is found in the X-ray structure[13] of the parent molecule of 3 (2,4,6-tri-*tert*-butylthiobenzaldehyde) for which the twist angle is 89° and in the twist angle of 65° estimated for 4 by dipole moment.[13,14]

It has to be emphasized that the splittings of the meta hydrogens in both the twisted radicals 3 and 4 (1.5 and 2.1 G) are even larger than those of the corresponding planar radicals 1 and 2. Whereas in the latters the splittings are a consequence of the $\pi-\pi$ delocalization of the unpaired electron upon the phenyl ring, this cannot be the case in 3 and 4 since the $\pi-\pi$ delocalization is minimized by the twisted conformational arrangement. The large meta splittings of 3 and 4 (Table I) are, on the other hand, a good example of a $\sigma-\pi$ delocalization mechanism. This mechanism is known to bring relatively high spin densities to the meta positions even when the phenyl ring is perpendicular to the sp^2 carbon bearing the unpaired electron. An example is the case of a perpendicular benzyl radical (1,1-di-*tert*-butylbenzyl) for which there is a substantial meta splitting (0.91 G).[15]

A comparison of the data of the two planar radicals 1 and 2 shows that the a_H values corresponding to the aromatic hydrogens in 2 are smaller than those of 1, in agreement with the observation[3-6] that the C=S moiety has a reduced ability, with respect to C=O, to delocalize the unpaired electron into the aromatic ring. For the same reason, the a_H value of the HC=S hydrogen in 2 is larger (13.1 G) than that of the hydrogen of the HCO group in 1 (12.1 G). The phenyl splittings of 2 are much larger than those of the thiobenzophenone anion radical;[6,7] this is consistent with the fact that conjugation occurs here with a single phenyl group and the spin density is not delocalized over two rings as in the case of thiobenzophenone radical anion.

The interaction of the unpaired electron with the hydrogen of the HC=X moiety is also expected to depend upon the conformational arrangement. In particular, the corresponding a_H splitting should be smaller for a planar structure (owing to the possible delocalization of the unpaired electron on the aromatic ring) than for a nonplanar structure. This accounts for the smaller value (13.1 G) of the HCS splitting in 2 with respect to that (15.6 G) in 3 where the *tert*-butyl group, as previously mentioned, forces the radical into an almost perpendicular conformation. This difference (2.5 G), however, is not as large as one might have expected, and furthermore, this trend is even reversed in the case of the ketyl radicals, where the HCO splitting is larger (12.1 G) in the case of 1 (planar) than in the case (10.3 G) of 4 (twisted).

These discrepancies can be, however, reconciled by the observation that the HCO splitting in a ketyl radical anion

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(and at a lesser extent also the HCS splitting of thioketyls) is extremely dependent upon the solvation.[1] In particular, the greater the hydrogen bonding with the solvent, the larger the value of the splitting (e.g., in the aprotic solvent *N,N*-dimethylformamide, the splitting of **1** is reduced to 8.5 G[16] from the 13.0 G observed in methanol[1]). Accordingly, it is conceivable that in the bulkier radical **3** the hydrogen bonding between the HCS moiety and the solvent (ethanol) is lower than in **2**. This would thus contribute to reduce the splitting of **3** with respect to **2**. The balance of the two opposite effects (i.e., the torsion that would increase the splitting and the lesser solvation that would reduce it) thus accounts for the rather moderate increment of the HCS splitting observed in **3** with respect to **2**. On the other hand, the torsion exerted by the *tert*-butyl groups upon the HCO in **4** is smaller than on the HCS moiety in **3**, owing to the shorter C=O bond distance. As a consequence, the contribution of the torsion in modifying the HC=X splitting is less important in **4** with respect to **1** (X = oxygen) than it is in **3** with respect to **2** (X = sulfur). Conversely, the greater polarity of HCO with respect to HCS would make the hydrogen bonding more efficent in **4** than in the corresponding thio radical **3**. In the ketyl radical **4**, the balance of the two opposite effects thus favors the contribution of solvation. This circumstance explains why the HCO splitting is smaller in **4** than in **1**, with a trend opposite to that expected solely on the basis of the conformational properties.

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Experimental Section

The ESR spectra were recorded with a Varian E3 ESR spectrometer. Photolysis was carried out with a 500-W high-pressure mercury lamp focused into the ESR cavity. The samples were degassed in a vacuum line by the usual thaw–freezing technique and sealed under vacuum. The *g* factor was measured by comparison with DPPH (2.0037) introduced in a capillary tube inside the sample under investigation.

The derivatives 2,4,6-tri-*tert*-butylbenzaldehyde and 2,4,6-tri-*tert*-buthylthiobenzaldehyde were prepared according to ref 14 and 12: MS, molecular ion at *m/e* 274.2289 (calcd 274.2297) and 290.2071 (calcd 290.2068), respectively.

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Registry No. **2**, 58712-13-3; benzenethiol, 100-53-8; 2,4,6-tri-*tert*-butylthiobenzaldehyde, 84543-57-7.

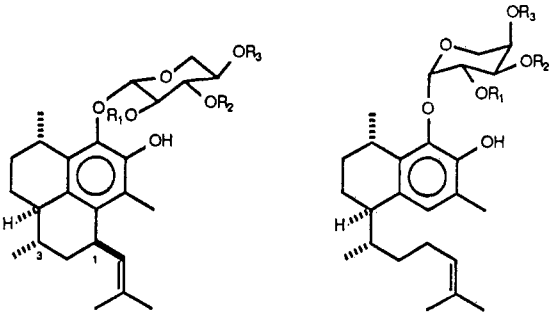
Communications

Total Synthesis of (-)-Pseudopterosin A

Summary: Pseudopterosin A has been synthesized, in optically active form, from (*S*)-(-)-limonene.

Sir: Pseudopterosins A–D (**1a–d**),[1,2] diterpene pentosides elaborated by the sea whip *Pseudopterogorgia elisabethae*, comprise a newly discovered family of biologically active marine natural products. Pharmacological studies[1] have shown them to possess antiinflammatory and analgesic activity with potencies comparable to that of indomethacin. Moreover, it appears that their mechanism of action is distinct from that of the cyclooxygenase-inhibiting antiinflammatory agents, making them particularly fascinating compounds from a biological standpoint. We record herein the first total synthesis of **1a**, in optically active form, by a route which should also lend itself to preparation of the related secopseudopterosins A–D (**2a–d**).[3]

(*S*)-(-)-Limonene was chosen as the starting material for this synthesis and converted into diols **3** by treatment with thexylborane according to the procedure of Brown.[4] The epimeric mixture was converted by routine operations into the hydroxy acid **4** and then lactonized to afford **5**, still as a mixture of epimers. Selenation–oxidation then gave



1a: $R_1 = R_2 = R_3 = H$
1b: $R_1 = Ac, R_2 = R_3 = H$
1c: $R_2 = Ac, R_1 = R_3 = H$
1d: $R_3 = Ac, R_1 = R_2 = H$

2a: $R_1 = R_2 = R_3 = H$
2b: $R_1 = Ac, R_2 = R_3 = H$
2c: $R_2 = Ac, R_1 = R_3 = H$
2d: $R_3 = Ac, R_1 = R_2 = H$

α-methylene lactone **6** (Scheme I).[5]

Having constructed the rigid bicyclic system **6** we were now in a position to establish the correct stereochemistry at that center destined to become C-3 of our target. Dropwise addition of **6** (in THF) to a mixture of vinylmagnesium bromide (2.25 equiv), copper(I) iodide (0.15 equiv), dimethyl sulfide (2 equiv), and trimethylsilyl chloride (5 equiv) in THF at -40 °C provided **7** in excellent yield as a single stereoisomer after aqueous workup. The presence of trimethylsilyl chloride[6] is essential to the success of this reaction as is the order of addition (lactone to vinylcopper reagent). Upon workup, hydrolysis of the initially formed silyl ketene acetal occurs with proton

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