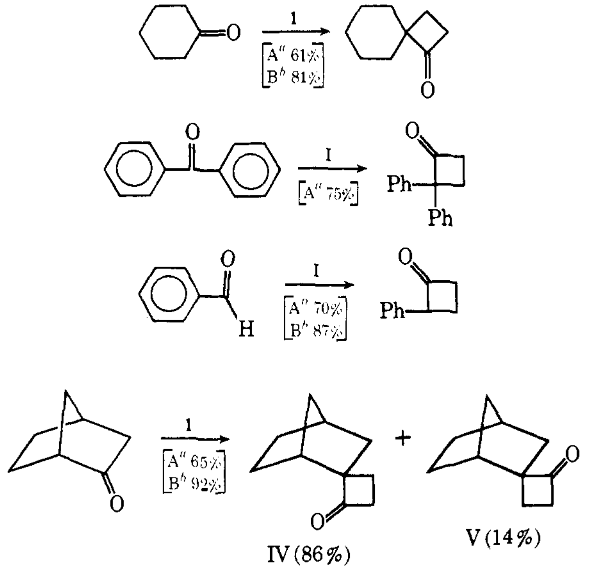
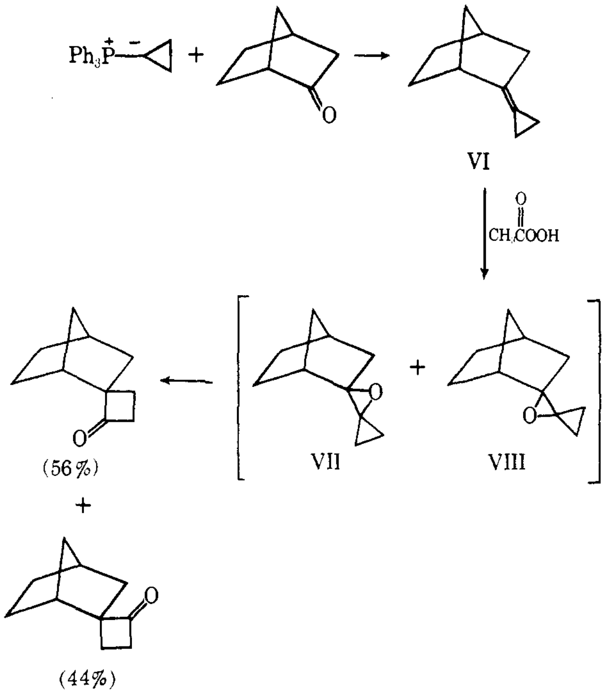
**Scheme III.** Reactions with Carbonyl Functions[c]



[a] Reaction performed by method A. [b] Reaction performed by method B. [c] Yields were determined by vpc analyses.

**Scheme IV.** Phosphorus Ylide Based Synthesis



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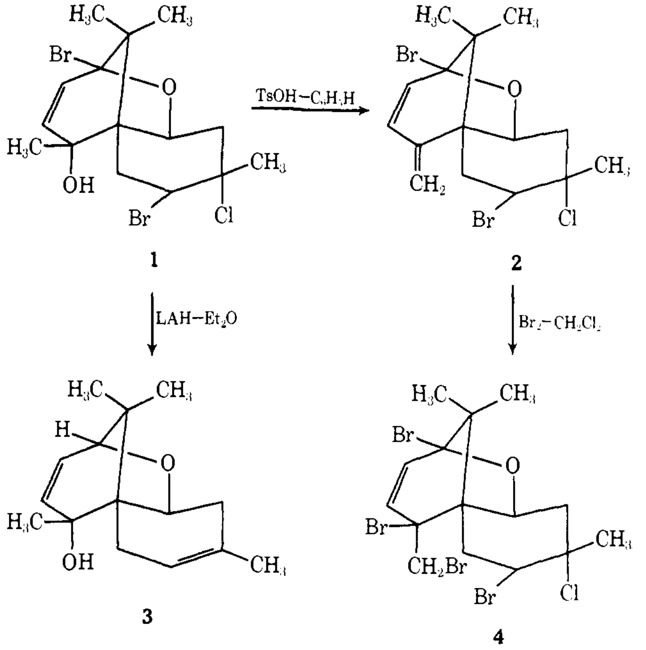
## Marine Natural Products. I. Pacifenol, a Rare Sesquiterpene Containing Bromine and Chlorine from the Red Alga, *Laurencia pacifica*

*Sir:*

Recent reports[1a–i] on the structures of secondary metabolites[2] from marine organisms illustrate significant differences in structural types over those isolated from terrestrial organisms. We have now isolated a structural variant from *Laurenica pacifica*, a red alga indigenous to the Pacific Ocean. The major compound (0.4% of the dried plant), pacifenol (**1**), is a representative of a sesquiterpene class containing the spiro[5.5]undecane skeleton.[3] Pacifenol is, to our knowledge, the first natural compound isolated which contains Br and Cl.

Silica gel chromatography of the ether-soluble portion of an alcoholic extract of the fresh seaweed yielded **1**:[4] $C_{15}H_{21}O_2BrCl$; mp 149–150.5° (petroleum ether); $m/e$ $M^+ - H_2O$ 408, 410, 412; high-resolution $m/e$ 410 = 409.9469 (calcd for $C_{15}H_{19}OBr^{79}Br^{81}Cl^{35}$: 409.9472).



The orthorhombic needles of **1** obtained by recrystallization from petroleum ether were subjected to X-ray crystallographic analysis. The cell constants, $a_0$ = 19.176 (17), $b_0$ = 12.11 (15), $c_0$ = 7.012 (7) Å, were determined from a least-squares fit of 12 carefully centered reflections using Mo K$\alpha$, radiation ($\lambda$ = 0.70926 Å). On the basis of systematic absences noted on precession and Weissenberg photographs, the space group was determined to be $P2_12_12_1$. The crystal density was 1.71 cm³, 1.74 g/cm³ being required for four molecules per unit cell.

The reflection data were collected under computer control using a Picker four-circle diffractometer with a 32.0-cm crystal to scintillation detector distance and a pulse height analyzer adjusted to accept 90% of a reflections intensity. Independent reflections (940)

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(2) J. D. Bu'Lock, "The Biosynthesis of Natural Products, an Introduction to Secondary Metabolites," McGraw-Hill, London, 1965.

(3) S. Ito, K. Endo, T. Yoshida, M. Yatagai, and M. Kodama, *Chem. Commun.*, 186 (1967).

(4) Acceptable elemental analyses were obtained for all new compounds. These compounds were characterized by ir and nmr spectra, which are consistent with the structures assigned.

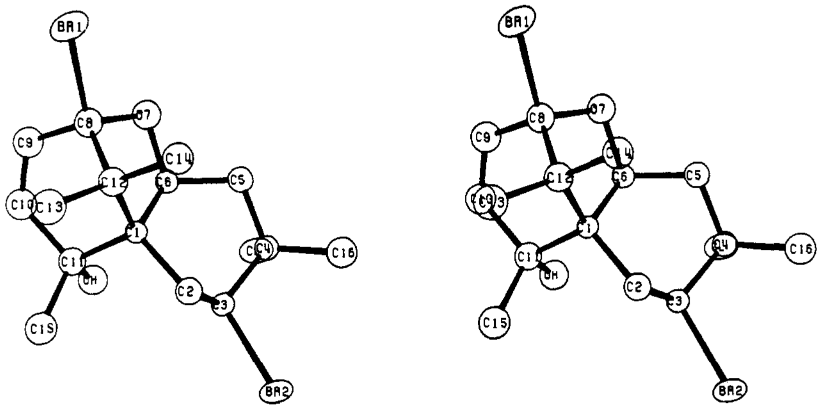


Figure 1. Pacifenol. There is a double bond between C-9 and C-10. This drawing is a stereopair.

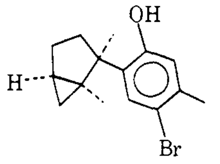
were measured with a maximum sin $\theta/\lambda$ of 0.49 $\text{Å}^{-1}$ using Mo-K$\alpha$ radiation made monochromatic by Bragg reflection from a graphite crystal.

Two bromine atoms were readily located in a three-dimensional Patterson map, and after improving their coordinates by two cyles of least-squares refinement, an electron density map revealed all but one of the remaining nonhydrogen atoms. Refinement by full-matrix least squares (the two bromine and the chlorine atoms were treated anisotropically) was straightforward, with only the 871 reflections which were above background by at least $3\sigma$ being included. Convergence to a final weighted residue ($wR$) of 6.4% for the absolute configuration shown in the figure occurred in 12 cycles. The enantiomorphic form gave $wR$ = 7.8% when treated in the same manner. Thus the absolute configuration given in the figure is certain at the 99.99% confidence level.[5] The standard deviation of an observation of unit weight is 1.82.

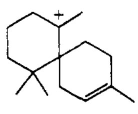
All bond lengths and angles are consistent with the accepted literature values, except for the bond $C_{11}$–OH which is 1.50 (1) Å or about 0.05 Å longer than expected. This is especially interesting in view of the fact that the mass spectrum of **1** always has as its highest mass peak the parent mass minus water; *vide supra*. Also of interest is the boat form adopted by the six-membered ring $C_1$–$C_6$. This ring can be flexed to give a chair, but an infavorable nonbonding interaction between Br-2 and C-14 (Figure 1) becomes prominent.

Treatment of **1** with toluenesulfonic acid in refluxing benzene readily gave pacifidiene[4] (**2**) in quantitative yield: mp 117–118.5°; $\lambda_{\max}^{\text{MeOH}}$ 237 nm ($\epsilon$ 8900). **1** exhibits a plain positive ORD curve but the lack of a near-uv absorbance prohibits us from obtaining acceptable data. Derivative **2**, however, shows a positive Cotton effect with $[\alpha]_D$ +13° and with a crest at 256 nm, $[\alpha]$ 2950°. Reduction of **1** with excess $LiAlH_4$ gave tridehalopacifenol[4] (**3**), an oil, $m/e$ 216 ($M^+ - H_2O$), but attempts at base-catalyzed elimination or treatment with $Zn$–$HOAc$–$Et_2O$ failed to yield any isolable compounds. The double bond in **1** was unreactive to $Br_2$–$CH_2Cl_2$, while **2** gave a dibromide which has been assigned structure **4** on spectral grounds.

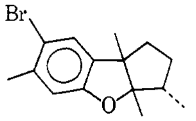
We also isolated from the *Laurencia* extract the known compound,[1f] laurinterol (**5**). The cooccurrence of **1** and **5** is significant in thinking about their biosynthesis. Both compounds can be derived formally from the ion **6**, a cyclization product of $\gamma$-bisabolene, which has been postulated[6] as the common precursor for several types of sesquiterpenes. Cyclization of **6** *via* an ether linkage leads to the tricyclic skeleton of **1**. A ring contraction of **6** by a 1,2 shift leads to the basic structural elements of **5**.



**5**



**6**



**7**

In view of the current concern with the presence of halogenated pesticides in the sea, it is interesting to find natural halogenated compounds occurring in *Laurencia*[1f,g] and some sponges.[1h,i] An implication of this occurrence is that natural metabolic mechanisms exist in the sea which can detoxify the compounds. It is already known that *Laurencia* is eaten by the sea hare,[7] *Aplysia*. As a result the sea hare contains aplysin[8] (**7**), which can also be isolated from a *Laurencia* species.[1f] Thus the compounds from *Laurencia* enter the food chain. We are at present evaluating the biological activity of **1** and its derivatives.

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