UV (MeOH) $\lambda_{max}$ ($\epsilon$) 280 nm (1740), 275 (1880), 225 (7230), 207 (16600); high-resolution EIMS, $m/z$ 304.167 (calcd for $C_{18}H_{24}O_4$, 304.167).

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**Registry No.** **3a**, 95189-16-5; **3b**, 95189-17-6; **4**, 95069-54-8; **5**, 95098-07-0; **6**, 95069-53-7.

# Synthesis of 3-Aryl-3,4-dihydroisocoumarins[1]

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The use of the *o*-tolyloxazoline as a common intermediate for the general synthesis of a series of 3-aryl-3,4-dihydroisocoumarins is described. The synthesis involves three single and convenient steps and provides the products in good yields. The products were characterized by analysis of their mass and high-resolution 500-MHz proton NMR spectral data.

## Introduction

Dihydroisocoumarins, similar to isocoumarins and coumarins, are a class of naturally occurring lactones exhibiting various biological activities.[3] 3-Substituted-3,4-dihydroisocoumarins occur as mycotoxins,[4,5] fungal metabolites,[6] and are a principal sweetness component of Japanese sweet tea.[7,8] Several synthetic methods have been reported for the syntheses of 3-substituted-3,4-dihydroisocoumarins,[5-13] but most require multistep syntheses. In connection with our interest in their sweetness property and their possible toxicity, we have developed a simple and convenient method for the synthesis of 3-aryl-3,4-dihydroisocoumarins.

## Results and Discussion

The method developed involves three steps (Scheme I). According to the method of Meyers et al.[14] for the synthesis of bromophenyloxazoline, reaction of *o*-toluyl chloride with 2-amino-2-methyl-1-propanol in methylene chloride at 0 °C under argon afforded *N*-(2-methyl-3-hydroxyprop-2-yl)-*o*-toluamide (1) in quantitative yield. Cyclization of 1 with thionyl chloride gave 2-(*o*-(tolyl)-4,4-dimethyl-2-oxazoline (**2**)[15] in 92% yield. Lithiation of **2** with *n*-butyllithium in ethyl ether at 0 °C proceeded rapidly to form the deep red anion **3** (Scheme I). Addition of aryl al-

**Scheme I**

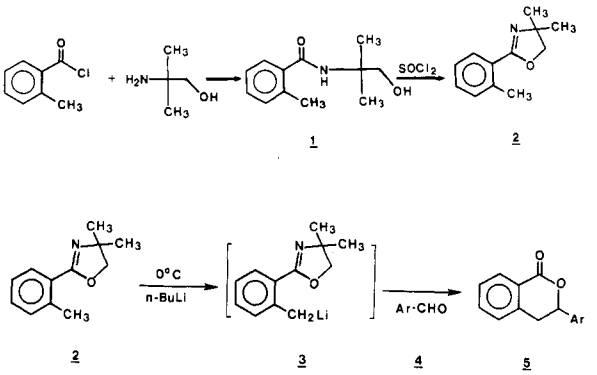


**Table I. Formation of 3-Aryl-3,4-dihydroisocoumarins from *o*-Tolyloxazoline and Aryl Aldehydes or 1-Acetylnaphthalene**

| compd | 3-aryl-3,4-dihydroisocoumarins | yield, % |
|---|---|---|
| benzaldehyde (**4a**) | 3-phenyl-3,4-dihydroisocoumarin (**5a**) | 72 |
| *p*-tolualdehyde (**4b**) | 3-*p*-tolyl-3,4-dihydroisocoumarin (**5b**) | 80 |
| *p*-methoxybenzaldehyde (**4c**) | 3-*p*-methoxy-3,4-dihydroisocoumarin (**5c**) | 65 |
| *o*-fluorobenzaldehyde (**4d**) | 3-*o*-fluoro-3,4-dihydroisocoumarin (**5d**) | 78 |
| 1-naphthaldehyde (**4e**) | 3-(1-naphthyl)-3,4-dihydroisocoumarin (**5e**) | 87 |
| 2-naphthaldehyde (**4f**) | 3-(2-naphthyl)-3,4-dihydroisocoumarin (**5f**) | 68 |
| 1-acetylnaphthalene (**4g**) | 3-methyl-3-(1-naphthyl)-3,4-dihydroisocoumarin (**5g**) | 56 |

(1) Presented in part at the 39th Southwest American Chemical Society Regional Meeting, Tulsa, OK, Dec, 1983.
(2) (a) National Center for Toxicological Research. (b) University of Arkansas at Little Rock. (c) Truman College.
(3) Steyn, P. S. In "Microsomal Toxins"; Ciegler, A., Kadis, S., Ajl, J. J., Eds.; Academic Press; New York, 1971; Vol. VI, pp 179–209.
(4) Bunge, I.; Derheimer, G.; Roschentaler, R. *Biochem. Biophys. Res. Commun.* **1978**, *83*(2), 398–405.
(5) Kraus, G. A. *J. Org. Chem.* **1981**, *46*, 201–202.
(6) Nozawa, K.; Makajima, S.; Yamada, M.; Kawai, K. I. *Chem. Pharm. Bull.* **1980**, *28*(5), 1622–1625.
(7) Takeuchi, N.; Ochi, K.; Murase, M.; Tobinaga, S. *J. Chem. Soc., Chem. Commun.* **1980**, *13*, 593–594.
(8) Takeuchi, N.; Murase, M.; Ochi, K.; Tobinaga, S. *Chem. Pharm. Bull.* **1980**, *28*(10), 3013–3019.
(9) Takeuchi, N.; Tobinaga, S. *Chem. Pharm. Bull.* **1980**, *28*(10), 3007–3012.
(10) Srivastava, J. N. *J. Indian Chem. Soc.* **1977**, *54*(9), 902–903.
(11) Yamato, M.; Kitamura, T.; Hashigaki, K.; Kuwano, Y.; Murakami, S.; Koyama, T. *Yakugaku Zasshi* **1972**, *92*(7), 850–853.
(12) Korte, D. E.; Hegedus, L. S.; Wirth, R. K. *J. Org. Chem.* **1977**, *42*(8), 1329–1335.
(13) Watanabe, M.; Sahara, M.; Kubo, M.; Furukawa, S.; Billedeau, R. J.; Snieckus, V. *J. Org. Chem.* **1984**, *49*, 742–474.
(14) Meyers, A. I.; Temple, D. L.; Haidukewych, D.; Mihelich, E. D. *J. Org. Chem.* **1974**, *39*(18), 2787–2793.
(15) Although oxazoline **2** has been reported for lithiation,[16] its synthesis procedure and physical data have never been described.
(16) Gschwend, H. W.; Hamadan, A. *J. Org. Chem.* **1975**, *40*(13), 2008–2009.
(17) Gunther, H. "NMR Spectroscopy, An Introduction"; translated by R. W. Gleason; John Wiley and Sons: New York, 1980; pp 70–76.

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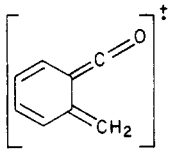
Table II. Chemical Shifts and Coupling Constants of the Benzylic Protons of 3-Aryl-3,4-dihydroisocoumarins[a]

| | chemical shift, ppm | | | coupling constant, Hz | | |
|---|---|---|---|---|---|---|
| no. | $H_3$ | $H_{4a}$ | $H_{4b}$ | $J_{3,4a}$ | $J_{3,4b}$ | $J_{4a,4b}$ |
| **5a** | 5.55 | 3.15 | 3.34 | 12.0 | 3.0 | 16.3 |
| **5b** | 5.50 | 3.10 | 3.32 | 12.0 | 3.0 | 16.3 |
| **5c** | 5.49 | 3.10 | 3.34 | 12.0 | 3.0 | 16.3 |
| **5d** | 5.85 | 3.17 | 3.33 | 12.0 | 3.4 | 16.3 |
| **5e** | 6.46 | 3.56 | 3.41 | 12.1 | 3.3 | 16.1 |
| **5f** | 5.86 | 3.50 | 3.37 | 12.1 | 3.1 | 16.6 |
| **5g** | | 3.95 | 3.60 | | | 16.7 |

[a] Determined with a Bruker WM 500 spectrometer. Samples were dissolved in acetone-$d_6$. Chemical shifts are reported in ppm downfield from internal tetramethylsilane. Coupling constants are based on first-order analysis.

dehydes (4) as electrophiles resulted in the desired 3-aryl-3,4-dihydroisocoumarins (5) in 65–87% yields without being affected significantly by steric or electronic effects. The results with six aryl aldehydes are summarized in Table I. It is apparent that this is a general synthetic method for the preparation of 3-aryl-3,4-dihydroisocoumarins.

Characterization of the products was achieved by mass and high-resolution proton NMR spectrometry. The mass spectra showed the molecular ions together with two common characteristic fragment ions at $m/z$ 118 and $m/z$ 90, presumably contributed from species **6** and **7**, respectively.




6

7

The high-resolution 500-MHz proton NMR spectra permitted unequivocal assignment of the structures with coupling patterns, homonuclear decoupling, and nuclear Overhauser enhancement techniques. In the case of **5d**, for example, the peak at 5.85 ppm assigned to $H_3$ exhibited a doublet of doublet pattern due to coupling with the two neighboring nonequivalent methylene protons whose resonances were found at 3.17 and 3.33 ppm, respectively. The peak assigned to $H_8$ was located at lowest field (8.01 ppm) due to the anisotropic effect of the peri carbonyl group and was exhibited by all the synthetic 3-aryl-3,4-dihydroisocoumarins. Chemical shifts and coupling constants of $H_3$, $H_{4a}$ and $H_{4b}$ in **5a–g** are listed in Table II. As expected, the chemical shifts of $H_{4a}$ and $H_{4b}$ are similar since they are remote from the 3-aryl substituent. $H_3$ of **5d** is shifted downfield by 0.3 ppm due to deshielding by the fluorine substituent. The 0.91 ppm downfield shift of $H_3$ in **5e** is due to the ring current of the 1-naphthyl substituent which contrasts with the much smaller shift caused by the 2-naphthyl substituent of **5f**.

On the basis of the mechanism, the reaction of the lithiated oxazoline **3** with an aryl ketone was expected to result in the corresponding 3,3-disubstituted-3,4-dihydroisocoumarin. Indeed, reaction of **3** with 1-acetylnaphthalene afforded 3-methyl-3-(1-naphthyl)-3,4-dihydroisocoumarin (**5g**) in 56% yield.

Because of the extent of $\pi$–$\pi$ conjugation, it is apparent that 3-arylisocoumarins are more stable than the respective 3-aryl-3,4-dihydroisocoumarins. Thus, dehydrogenation of the latter is expected to produce the former readily. Therefore, we believe that the method described in this paper will be general for synthesis of 3-aryl-3,4-dihydroisocoumarins and 3-arylisocoumarins.

## Experimental Section

**2-(*o*-Tolyl)-4,4-dimethyl-2-oxazoline (2).** A mixture of *o*-toluic acid (68.0 g, 0.5 mol) and thionyl chloride (180 g, 1.5 mol) was stirred at ambient temperature under an argon atmosphere for 18 h. The excess thionyl chloride was removed by distillation and the *o*-toluoyl chloride was distilled from the residue as colorless oil (69.6 g, 92% yield). The *o*-toluoyl chloride (67.7 g, 0.44 mol) was dissolved in methylene chloride (250 mL) and added dropwise to a solution of 2-amino-2-methyl-1-propanol (78.0 g, 0.88 mol) in methylene chloride (250 mL) at 0 °C. After the addition was complete, the reaction was stirred for another 30 min. The precipitate, identified as the amine hydrochloride, was removed by suction filtration. The filtrate was evaporated and the resulting residue was dried under vacuum, affording *N*-(2-methyl-3-hydroxyprop-2-yl)-*o*-toluamide (1) in quantitative yield (91.0 g, 0.44 mol): NMR ($CDCl_3$) 1.08 (s, 6, $CH_3$), 2.21 (s, 3, $CH_3$), 3.22 (s, 2, $CH_2$), and 6.80–7.06 ppm (m, 4, aromatic).

Thionyl chloride (150 mL) was added dropwise to the amide 1 (91.0 g, 0.44 mol) under argon atmosphere. After the solution was stirred for 1 h, methanol (150 mL) was added to destroy the excess thionyl chloride. The reaction mixture was then poured into 1 L of alkaine solution containing 20 g of $KHCO_3$. After the addition of 50 g of KOH pellet, the alkaline solution was extracted twice with ethyl ether (2 × 500 mL). The ethereal layer was separated and dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure affording oxazoline **2** as a light yellow oil (20 g, 92% yield): mass spectrum (70 eV), $m/z$ 189 ($M^+$) and 174 ($M^+ - CH_3$); NMR ($CDCl_3$) 1.24 (s, 6, $CH_3$), 3.80 (s, 2, $CH_3$), 6.84 (m, 3, aromatic), and 7.40 ppm (d, 1, aromatic). The product **2** is sufficiently pure for further reaction.

**General Procedure for Preparation of 3-Aryl-3,4-dihydroisocoumarins.** The oxazoline **2** (10 mmol) dissolved in anhydrous ethyl ether (30 mL) was cooled to <0 °C with an ice–salt bath under argon atmosphere. A solution of *n*-butyllithium (10 mmol) in ethyl ether (20 mL) was added slowly to maintain the temperature below 0 °C. The deep red anion **3** was produced readily. After stirring for 1 h, aryl aldehyde (or the aryl ketone) (10 mmol) dissolved in ethyl ether (30 mL) was added. The resulting solution was stirred overnight at room temperature. The reaction mixture was hydrolyzed by refluxing with a 1 N HCl (70 mL) for 1 h and was then partitioned between ethyl ether and water. The organic layer was separated, dried over $MgSO_4$, and the solvent was removed under reduced pressure. Purification of the product from the residue was carried out as indicated by the entries below for the separate compounds.

**3-Phenyl-3,4-dihydroisocoumarin (5a).** The residue was chromatographed on Florisil and eluted with benzene, affording pure **5a** in 72% yield: mp 90–92 °C (lit.[18] mp 88–90 °C); UV spectrum $\lambda_{max}$ 239 and 279 m; IR (nujol) 1720 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 224 ($M^+$), 118, 90; NMR (acetone-$d_6$) 7.31 (d, 1, $J_{5,6}$ = 7.7 Hz, $H_5$), 7.38 (d, 1, $J_{3',4'}$ = 8.2 Hz, $H_{4'}$), 7.43 (m, 2, $H_{6,7}$), 7.48 (apparent d, 2, $H_{2',6'}$), 7.58 (5, s, $H_{3',5'}$), 8.09 ppm (d, 1, $J_{7,8}$ = 7.7 Hz, $H_8$) and Table II.

**3-(*p*-Tolyl)-3,4-dihydroisocoumarin (5b).** After the crude product was purified by column chromatography over Florisil with benzene as the eluant, pure **5b** was obtained in 80% yield: mp 95–96 °C; UV $\lambda_{max}$ 242 and 280 nm; IR (nujol) 1715 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 236 ($M^+$), 208, ($M^+ - CO$), 195, 194, 179, 165; NMR (acetone-$d_6$) 2.37 (s, 3, $CH_3$), 7.24 (d, 2, $J_{2',3'}$ = 7.9 Hz, $H_{3',5'}$), 7.31 (d, 1, $J_{5,6}$ = 7.4 Hz, $H_5$), 7.36 (d, 2, $H_{2',6'}$), 7.43 (t, 1, $H_7$), 7.58 (t, 1, $J_{6,7}$ = 8.9 Hz, $H_6$), 8.09 ppm (d, 1, $J_{7,8}$ = 7.9 Hz, $H_8$) and Table II. Anal. Calcd for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.88; H, 6.07.

**3-(*p*-Methoxyphenyl)-3,4-dihydroisocoumarin (5c).** Pure **5c** was obtained as colorless plates (65% yield) by crystallization of the crude product from methanol: mp 108–109 °C; UV $\lambda_{max}$ 242 and 272 nm; IR (nujol) 1705 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 252 ($M^+$), 208 ($M^+ - CO_2$), 118; NMR (acetone-$d_6$) 3.82 (s, 3, $CH_3$), 6.95 (dd, 2, $J_{2',3'} = J_{5',6'}$ = 8.6 Hz, $H_{3',5'}$), 7.31 (d, 1, $J_{5,6}$ = 7.7 Hz, $H_5$), 7.40 (dd, 2, $H_{2',6'}$), 7.43 (d, 1, $J_{6,7}$ = 8.2 Hz, $H_7$), 7.77 (t, 1, $H_6$), 8.08 ppm (d, 1, $J_{7,8}$ = 7.7 Hz, $H_8$) and Table II. Anal. Calcd for $C_{16}H_{14}O_3$: C, 75.58; H, 5.55. Found: C, 75.55; H, 5.70.

(18) Sen, A. B.; Kulkarni, Y. D. *J. Indian Chem. Soc.* **1957**, *34*, 467–470.

**3-(o-Fluorophenyl)-3,4-dihydroisocoumarin (5d).** The crude product was chromatographed on Florisil and eluted with benzene, providing pure **5d** as a yellowish oil (78% yield) which solidified on standing: UV $\lambda_{max}$ 247 and 279 nm; IR (nujol) 1730 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 242 ($M^+$), 197, 196, 183; NMR (acetone-$d_6$) 7.08 (5, 1, $J_{3',4'}$ = 8.2 Hz, $J_{3',F}$ = 10.3 Hz, $H_{3'}$), 7.22 (5, 1, $J_{5',6'}$ = 7.3 Hz, $H_{6'}$), 7.32 (d, 1, $J_{5,6}$ = 7.7 Hz, $H_5$), 7.35 (m, 1, $H_{4'}$), 7.44 (t, 1, $J_{4',5'}$ = 7.7 Hz, $H_{5'}$), 7.57–7.64 (m, 2, $H_{6,7}$), 8.01 ppm (d, 1, $J_{7,8}$ = 7.7 Hz, $H_8$) and Table II. Anal. Calcd for $C_{15}H_{11}FO_2$: C, 74.37; H, 4.58; O, 13.21. Found: C, 74.34; H, 4.59; O, 13.50.

**3-(1-Naphthyl)-3,4-dihydroisocoumarin (5e).** Pure **5e** was obtained as colorless needles (87% yield) by crystallization of the crude product from methanol: mp 155–156 °C; UV $\lambda_{max}$ 233 and 270 nm; IR (nujol) 1710 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 272 ($M^+$), 229, 228, 215; NMR (acetone-$d_6$) 7.44 (d, 1 H), 7.50 (t, 1 H), 7.57 (m, 3 H), 7.66 (t, 1 H), 7.80 (d, 1 H), 7.95 (d, 1 H), 7.90 (dd, 1 H), 8.10 (d, 1 H), 8.26 ppm (d, 1 H) and Table II. Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 83.03; H, 5.23.

**3-(2-Naphthyl)-3,4-dihydroisocoumarin (5f).** Crystallization of the crude product from methanol afforded pure **5f** as colorless plates (68% yield): mp 137–138 °C; UV $\lambda_{max}$ 238 and 272 nm; IR (nujol) 1710 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 274 ($M^+$), 229, 228, 155; NMR spectrum (acetone-$d_6$) 7.47 (d, 1, $J_{5,6}$ = 7.7 Hz, $H_5$), 7.50 (t, 1, $J_{6,7} = J_{7,8}$ = 7.6 Hz, $H_7$), 7.57 (m, 2, $H_{6',7'}$), 7.67 (dt, 1, $H_6$), 7.74 (dd, 1, $J_{3',4'}$ = 8.5 Hz, $J_{1',3'}$ = 1.8 Hz, $H_{3'}$), 7.97 (m, 2, $H_{5',8'}$), 8.01 (d, 1, $H_{4'}$), 8.08 (d, 1, $H_8$), 8.09 ppm (d, 1, $H_{1'}$) and Table II. Anal. Calcd for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 82.93; H, 5.10.

**3-Methyl-3-(1-naphthyl)-3,4-dihydroisocoumarin (5g).** Pure **5g** was obtained by column chromatography of the crude product on Florisil eluted with benzene as a yellowish oil (56% yield): UV $\lambda_{max}$ 232 and 288 nm; IR (nujol) 1710 $cm^{-1}$; mass spectrum (70 eV), $m/z$ 298 ($M^+$), 273 ($M^+ - CH_3$), 270 ($M^+ - CO$), 255, 245; NMR spectrum (acetone-$d_6$) 2.08 (s, 3, $CH_3$), 7.28 (m, 2 H), 7.35 (d, 1 H), 7.40 (d, 1 H), 7.52 (m, 4 H), 7.74 (d, 1 H), 7.85 (d, 1 H), 7.88 ppm (d, 1 H) and Table II. Anal. Calcd for $C_{20}H_{16}O_2$: C, 83.31; H, 5.60. Found: C, 83.11; H, 5.73.

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**Registry No.** **1**, 95217-40-6; **2**, 71885-44-4; **3**, 78482-09-4; **4a**, 100-52-7; **4b**, 104-87-0; **4c**, 123-11-5; **4d**, 446-52-6; **4e**, 66-77-3; **4f**, 66-99-9; **4g**, 941-98-0; **5a**, 2674-44-4; **5b**, 95217-41-7; **5c**, 37568-81-3; **5d**, 95217-42-8; **5e**, 83640-59-9; **5f**, 83640-60-2; **5g**, 95217-43-9; *o*-toluoyl chloride, 933-88-0; 2-amino-2-methyl-1-propanal, 124-68-5; *o*-toluic acid, 118-90-1.

# New Halogenated Diterpenes from the Red Alga *Laurencia perforata*

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The red alga *Laurencia perforata* contains a variety of secondary metabolites, some of which have previously been described from other sources. We report here the isolation and structural determination of three new diterpenoids. The bicarbocyclic diterpene **1** was shown to be related with the also isolated, and previously known, isoaplysin-20 (**2**). The structures of the two more polar diterpenes isolated from the extract were shown to be 3,15-dibromo-7,16-dihydroxyisopimar-9(11)-ene (**5**) and 3,15-dibromo-7,12,16-trihydroxyisopimar-9(11)-ene (**7**). Extensive $^1H$ NMR decoupling studies and some degradative experiments were used to establish the structures.

The present work is a part of our results on the chemical analysis carried out on different collections of the seaweed *Laurencia perforata* in the Canary and Madeira archipelagos. The diterpenoid components isolated were **1**, **2**, **5**, and **7**, all of which, with the exception of the dihydroxybrominated **2**, known as isoaplysin-20 and isolated from the mollusc *Aplysia kurodai*,[1] are presented for the first time in this work.

The least polar diterpenoid proved to be the bicarbocyclic compound **1**, which was isolated by successive quick chromatographies in silica gel using petroleum ether–ethyl acetate (1%) as eluent. Compound **1** proved identical with one obtained in quantitative yield by heterolytic fragmentation induced on the tosylated **4** by base treatment.[2]

Compound **5**, 3,15-dibromo-7,16-dihydroxyisopimar-9-(11)-ene, was isolated by chromatographic purification from the most polar fractions of the extract. The $^1H$ and $^{13}C$ NMR spectra are presented in Tables I and II, together with other derivatives and related compounds.

Treatment of **5** with acetic anhydride–pyridine gave the diacetate **6**, which was isolated as an oil. Compound **6** afforded in quantitative yield the epoxy derivative **9** by treatment with potassium carbonate in methanol, which was further oxidized with pyridinium chlorochromate to give the monoketone **10** as the sole reaction product. The oxidation of the epoxy alcohol **9** with chromic anhydride in acetone gave the enedione **11** (Chart I).

Reduction of **5** with Zn–AcOH afforded a mixture of products from which compound **12** was isolated as a major component, exhibiting an olefinic ABX system in its $^1H$ NMR spectrum.

The existence of three quaternary carbons, as well as the vinylic carbon, which can be observed in the $^{13}C$ NMR spectra of the natural product and derivatives (Table II) and the tricarbocyclic nature of same, suggested a pimarane skeleton (**i**) as a basis on which to support the methyl and ethyl appendages observed.[4]

(1) (a) Yamamura, S.; Tereda, Y. *Tetrahedron Lett.* **1977**, 2171. (b) Imamura, P. M.; Rüveda, E. A. *J. Org. Chem.* **1980**, *45*, 510. (c) Nishizawa, M.; Takenaka, H.; Hirotsu, K.; Higuchi, T.; Hayashi, Y. *J. Am. Chem. Soc.* **1984**, *106*, 4290.

(2) The possibility that **1** is an artefact cannot be excluded, despite the fact that it was isolated by extraction from the freshly gathered alga with organic solvents at room temperature. Isoaplysin-20 (**2**) submitted to the extraction conditions of the alga did not undergo transformation to compound **1**.

(3) We thank Prof. S. Yamamura for a small sample of isoaplysin-20 for comparative purposes.

(4) Devon, T. K.; Scott, A. I. "Handbook of Naturally Occurring Compound", Academic Press: New York, 1972; Vol. II.

0022-3263/85/1950-1261$01.50/0 