A Biomimetic Approach to the Synthesis of *Laurencia* Metabolites. Synthesis of 10-Bromo-α-chamigrene

L. E. Wolinsky and D. J. Faulkner*

Scripps Institution of Oceanography, La Jolla, California 92037

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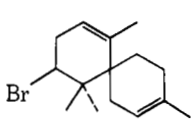
A number of halogenated sesquiterpenes based on the chamigrene skeleton have been isolated from red algae of the genus *Laurencia*. We have synthesized the simplest halogenated chamigrene, 10-bromo-α-chamigrene (1). The bromonium ion initiated cyclization of geranylacetone (22) gave the vinyl ether 23, which underwent acid-catalyzed rearrangement to the bromo ketone 24. The bromo ketone was converted into the vinyl alcohol 25, which was cyclized under acidic conditions to obtain 10-bromo-α-chamigrene (1). We have studied the efficacy of various brominating reagents in the bromonium ion initiated cyclization of geranyl acetate (15).

An interesting group of halogenated sesquiterpenes whose structures are based on the chamigrene skeleton have been isolated from various species of red algae of the genus *Laurencia* (Rhodomalaceae, Rhodophyta).[1] Although several schemes for the biosynthesis of halogenated chamigrenes have been proposed,[2] they all involve a bromonium ion initiated cyclization of a suitable precursor. We wish to report an investigation of bromonium ion initiated cyclization reactions which has culminated in a synthesis of 10-bromo-α-chamigrene (1).

Although 10-bromo-α-chamigrene (1) has not been reported as a natural product, we believe that it may be regarded as the simplest bicyclic precursor to all other halogenated chamigrenes.[18] For example, 10-bromo-α-chamigrene (1) can be a precursor of both the epoxide 2[3] and the dibromide 3[4], as well as more complex chamigrenes such as prepacifenol (4)[5], pacifenol (5),[6] prepacifenol epoxide (6),[7] johnstonol (7),[8] elatol (8),[9] and acetoxyintracatol (9).[10]



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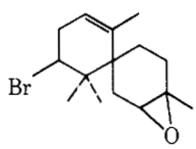

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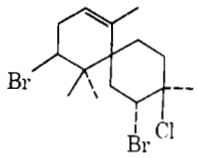

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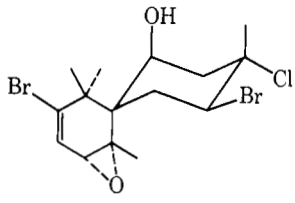

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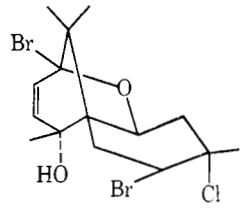

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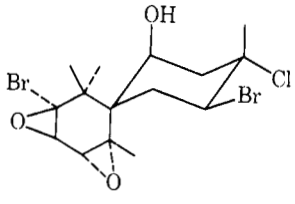

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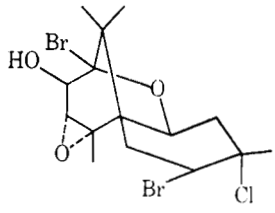

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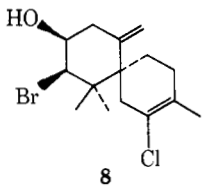

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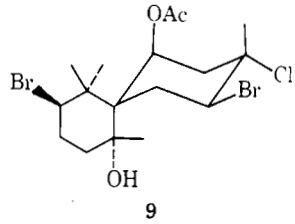

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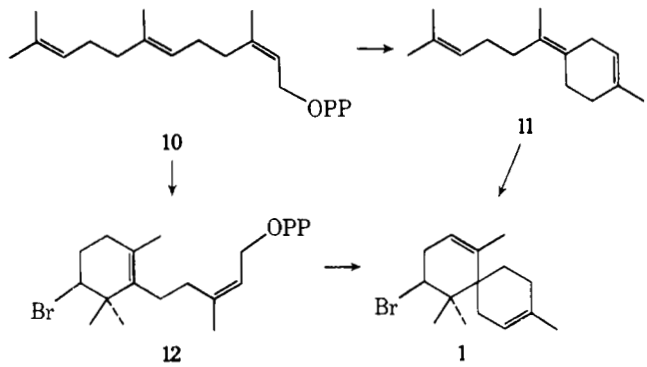
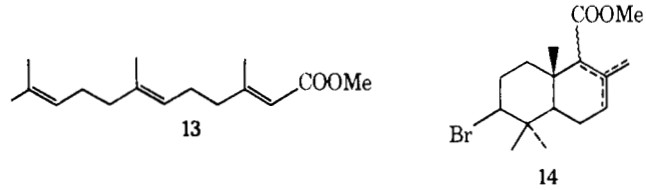
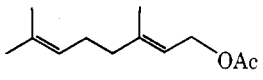
It is possible to envisage two distinct biosynthetic routes from farnesyl pyrophosphate (10) to 10-bromo-α-chamigrene (1) by way of either γ-bisabolene (11) or the brominated monocyclofarnesol (12). We have investigated synthetic routes which involve the use of both types of intermediate.





A bromonium ion induced cyclization was first observed by van Tamelen and Hessler,[11] who isolated bicyclic bromo esters 14 as a minor product from the treatment of methyl farnesoate (13) with *N*-bromosuccinimide in aqueous tetrahydrofuran. Sutherland et al.[12] have made use of the same reagent for the cyclization of humulene, a medium-ring sesquiterpene. The higher yields in the cyclization of medium-ring compounds were made possible by the close proximity of the participating olefinic bonds.

In order to compare the efficacy of various brominating reagents, we investigated the bromonium ion initiated cyclization of geranyl acetate. We were unable to obtain any trace of cyclized material by treatment of geranyl acetate (15) with *N*-bromosuccinimide in aqueous glyme. The intermediate bromonium ion 16 was quenched by water to give the bromohydrin 17 before cyclization could occur. We therefore investigated the use of reagent systems in which there were no nucleophiles present to trap the intermediate bromonium ion 16. Treatment of geranyl acetate (>98% *E* isomer by vpc) (15) with 1 equiv each of bromine and stannic bromide in nitromethane at 0°C for 5 min gave, after work-up with sodium bicarbonate solution, a viscous oil from which crystals of the cyclized bromoacetate 19 were obtained in 16% yield after chromatography. The cyclized product 19 was shown by mass spectrometry to have the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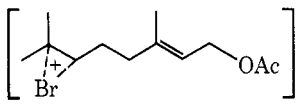
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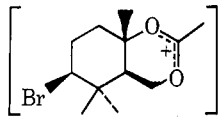
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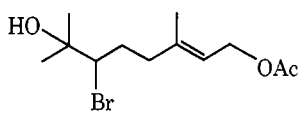
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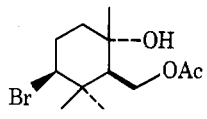
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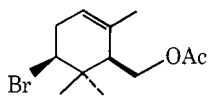
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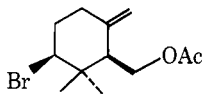
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molecular formula $C_{12}H_{21}O_3Br$, isomeric with the bromohydrin **17**. The chemical shifts of the three methyl singlets at δ 0.98, 1.15, and 1.22 ppm in the NMR spectrum of **19** clearly indicated that the methyl groups were no longer attached to olefinic carbon atoms. The NMR spectrum of **19** contained an acetoxy signal at 2.05 ppm and a double doublet at 4.00 ppm (J = 12 and 5 Hz) due to a proton α to bromine and a two-proton multiplet at 4.38 ppm due to the methylene group bearing the acetoxy group. Examination of the NMR spectra of *Laurencia* metabolites reveals that the double doublet signal at 4–5 ppm is characteristic of 1,1-disubstituted 2 (equatorial) bromocyclohexanes. Clearly, the expected cyclization had occurred.

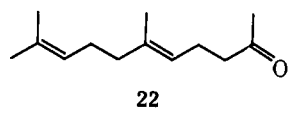
Since the bromoacetate **19** contained a tertiary alcohol functionality (ir 3480 cm^{-1}) and water had been rigorously excluded from the reaction mixture, we propose that the initial product was the bicyclic ion **18**, which was hydrolyzed during work-up. The stereochemistry shown for the bromoacetate **19** is an outcome of this reaction mechanism.

During the purification of the bromoacetate **19**, we had obtained fairly large quantities of materials having two bromine atoms, indicating normal bromine additions. We therefore attempted to remove bromide ion as it was produced. Treatment of geranyl acetate (**15**) with equimolar amounts of bromine and silver fluoroborate in nitromethane solution at 0°C resulted in an immediate precipitation of silver bromide. The bromoacetate **19** was obtained in 20% yield.

Treatment of the bromoacetate **19** with p-toluenesulfonic acid in refluxing benzene gave an inseparable mixture of dehydration products in 77% yield. The NMR spectrum of the mixture of olefins contained signals at δ 4.77 and 5.30 due to two methylene protons and at 5.35 ppm, indicative of a trisubstituted olefinic bond. The product was therefore a 2:1 mixture of the olefins **20** and **21**. At the time we considered this result to be a severe setback, since we required a tetrasubstituted olefinic bond for any synthesis of a spiro bicyclic system. Fortunately, application of the same series of reactions to geranylacetone gave the desired product.

Geranylacetone (**22**) was treated with 1 equiv each of bromine and silver fluoroborate in nitromethane at 0°C to obtain a bicyclic vinyl ether **23** in 20% yield. The NMR spectrum of the vinyl ether **23** contained four methyl singlets at δ 0.92, 1.05, 1.16, and 1.65, a double doublet at 4.00 ppm due to the proton α to bromine, and a triplet at 4.47 ppm due to the vinyl proton.

Rearrangement of the vinyl ether **23** using p-toluenesulfonic acid in benzene solution gave the desired ketone **24** (ir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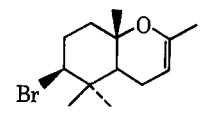
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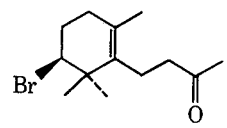
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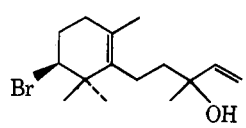
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1725 cm^{-1}) in 73% yield. The NMR spectrum contained a six-proton singlet at δ 1.11, a vinyl methyl signal at 1.54 ppm, and an acetyl signal at 2.03 ppm but no trace of a vinyl proton signal. Thus the rearranged product must contain a tetrasubstituted olefinic bond.

The synthesis of a chamigrene required the addition of a two-carbon unit. The addition of vinylmagnesium bromide to the ketone **24** in tetrahydrofuran solution gave the vinyl alcohol **25** in 91% yield. For the purposes of the following reaction, the vinyl alcohol **25** may be regarded as equivalent to the monocyclofarnesol. The vinyl alcohol **25** was treated with p-toluenesulfonic acid in benzene solution for 15 min to obtain a mixture of brominated hydrocarbons. The major product was shown to be 10-bromo-α-chamigrene (**1**).

We have not been able to determine the stereochemistry of the 10-bromo-α-chamigrene (**1**) formed in the reaction. By analogy with spiro-cyclization reactions involving carbanions, we might expect the newly formed bond to be trans to the bromine. On the other hand, an x-ray crystallographic study of elatol (**8**) and acetoxyintracatol (**9**) indicated that the opposite stereochemical relationship might occur in the natural product. There is, however, no proof that all the natural bromochamigrenes have the same stereochemical relationship between the bromine on one ring and the bromine and chlorine on the second ring, or that the two hypothetical 10-bromo-α-chamigrenes are separable by VPC or can be distinguished by spectroscopic methods. Examination of combined gas chromatogram–mass spectrometer data suggested that the synthetic cyclization product contained only one isomer of 10-bromo-α-chamigrene and that the gas chromatographic retention times, mass spectral fragmentation pattern, and 220-MHz NMR spectrum were identical with those of a sample obtained by reductive dehalogenation of the *Laurencia* metabolite **3**.[13]

We have also investigated the bromocyclization reaction of (*E*)-γ-bisabolene (**11**), which had been prepared in this laboratory.[14] Although we investigated the use of several reagents, including bromine–stannic bromide and bromine–silver tetrafluoroborate, we were unable to detect any 10-bromo-α-chamigrene among the complex mixtures of products.

Because of the catalytic properties of enzymes, it is difficult to determine the biosynthetic significance of these experiments. We have shown that without the benefit of enzymes to direct the bromination to the correct olefinic bond and to control the stereochemistry of the substrate, the biosynthesis of the bromochamigrenes is more likely to occur through the intermediacy of a bromomonocyclofarnesol than via γ-bisabolene. The recent discovery of a brominated natural product having the carbon skeleton of monocyclofarnesol provides some support for this biosynthetic route.[15]

Experimental Section

Commercially available chemicals were used without further purification unless otherwise stated. All solvents were either analar grade or redistilled prior to use. Melting points were measured on

a Fisher-Johns apparatus and are uncorrected. NMR spectra were recorded on Varian HR-220 or EM-360 spectrometers; chemical shifts are expressed as values in parts per million relative to tetramethylsilane (0). Infrared spectra were recorded on a Perkin-Elmer 700 spectrometer. Gas chromatographic analyses were performed on a Hewlett-Packard 402 instrument. Mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High-resolution mass spectra were measured by Beth Irwin, Department of Chemistry, UCLA.

5-Bromo-1-acetoxymethyl-2,6,6-trimethyl-2-hydroxycyclohexane (19) (Procedure A). A 250-ml, three-necked, round-bottom flask equipped with a low-temperature thermometer, a magnetic stirrer, and a gas inlet tube was flushed with argon. A solution of *trans*-geranylacetate[16] (>98% *E* isomer) (5.88 g, 330 mmol) in anhydrous nitromethane (30 ml) was added via a syringe. The solution was cooled to −20° using a dry ice–carbon tetrachloride bath, and a nitromethane solution of tin(IV) bromide (13.14 g, 30 mmol) and bromine (30 ml, 1 M, 30 mmol) was added dropwise. The temperature was maintained below −10° during the addition. After 30 min, the solution was poured into sodium bicarbonate (100 ml) and ethyl ether (100 ml). The ether phase was separated and washed successively with saturated sodium bicarbonate solution and saturated brine. The ether phase was dried over anhydrous magnesium sulfate. Removal of the solvent by distillation under high vacuum afforded 11.18 g of a crude yellow oil. Thin layer chromatography on silica gel in 5% ethyl ether–petroleum ether (bp 30–60°) and 5:1 benzene–ethyl acetate showed the presence of many compounds. The 220-MHz NMR of this crude material showed several high-field methyl signals appropriate for a cyclic product. GLC analysis (6 ft, 2% SP2401 on Chromosorb W) showed many products, with one major product having a retention time of 6.8 min at 160°. The crude material was passed through a short Florisil column (6 × 2 in.) with ethyl ether to remove any tin compounds. The material collected from this column was carefully chromatographed on silica gel chromatography. Crude material (9.46 g) was placed on 100 g of silica gel (Grace Chemical) and eluted with a solvent gradient from petroleum ether to ethyl ether to chloroform and ethyl acetate. The majority of the material was found in two fractions. The less polar of the two fractions (R_f 0.90 in 50% ethyl ether–hexane) amounted to 1.2 g of a yellow oil. The 60-MHz NMR of this mixture indicated an acyclic compound. By mass spectrometry, this fraction was shown to contain dibrominated compounds. This fraction was disregarded. The second more polar fraction had R_f 0.20 in 50% ethyl ether–hexane. Upon standing, this fraction crystallized to give the desired bromoacetate **19**, which was recrystallized from petroleum ether: mp 73°; yield 1.4 g (16%); ir ($CHCl_3$) 3478, 1724, 1242 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 0.98 (s, 3 H), 1.15 (s, 3 H), 1.22 (s, 3 H), 2.04 (s, 3 H), 2.72 (s, broad, 1 H), 4.00 (dd, J = 12, 5 Hz, 1 H), 4.38 (dd, 2 H). Anal. Calcd for $C_{12}H_{21}BrO_3$: C, 49.15; H, 7.22; Br, 27.25. Found: C, 49.09; H, 7.31; Br, 27.14.

5-Bromo-1-acetoxymethyl-2,6,6-trimethyl-2-hydroxycyclohexane (19) (Procedure B). A 50-ml, three-neck, round-bottom flask, equipped with a magnetic stirrer, a low-temperature thermometer, and a gas inlet tube was flushed with argon. Silver tetrafluoroborate (197 mg, 1 mmol) was dissolved in anhydrous nitromethane (5 ml) and added to the reaction vessel. The mixture was cooled to 0° using an ice–methanol bath, following which a solution of bromine (1 ml, 1 mmol) in nitromethane was added. The resulting orange solution was stirred for 5 min. A nitromethane solution of geranylacetate (196 mg, 1 mmol) was added dropwise to obtain a precipitate of silver bromide. The reaction mixture was stirred for another 5 min at 0°, then quenched by addition of cold saturated sodium bicarbonate solution (50 ml) and extraction with ethyl ether (2 × 50 ml). The organic layer was dried and the solvent removed to yield a pale yellow oil. The GLC trace (2% SP2401 on Chromosorb G, 160°) showed two major peaks, one of which was the desired cyclic hydroxyacetate. This method gave a higher yield (judged by the GLC trace) than procedure A. The oil obtained was submitted to silica gel chromatography, to obtain the bromoacetate as white prisms, yield 58.4 mg (20%). All spectral properties were identical with those of the sample prepared by alternate route A.

Dehydration of Bromoacetate 19. Recrystallized bromoacetate 19 (20 mg, 0.7 mmol) was dissolved in anhydrous benzene (0.5 ml). A few crystals of *p*-toluenesulfonic acid monohydrate were added and the mixture was refluxed for 2 hr. The reaction was followed by thin layer silica gel chromatography (50% ethyl ether–petroleum ether). After 2 h, the purple-red solution was cooled and benzene (25 ml) was added. The mixture was carefully washed with sodium bicarbonate solution (2 × 50 ml). The benzene layer was then dried over anhydrous magnesium sulfate and the solvent removed under vacuum. This gave a mixture of dehydration products: yield 14 mg (77%). GLC analysis of the oil (6 ft Silar 10 CP glass column at 120°) showed two major peaks at retention times of approximately 10 min. It was assumed that these two products must be double bond isomers, since the mass spectra of the two peaks were almost identical. Ir (CCl_4) 1740, 1640 weak, 1240 cm^{-1}; NMR (220 MHz) δ 0.95 (s, 3 H), 1.15 (s, 3 H), 1.68 (s, 3 H), 2.02 (s, 3 H), 2.21 (m, 2 H), 2.59 (m, 2 H), 4.20 (m, 2 H), 4.44 (dd, 1 H), 5.35 (broad, 1 H). The NMR also contained what appeared to be two vinyl proton signals of an exocyclic double bond at δ 4.77 and 5.30. From the integration of the NMR and the GLC traces, it was concluded that the oil was an isomeric mixture of the two compounds 1-bromo-3-acetoxymethyl-2,2,4-trimethyl-4-cyclohexene (**20**) and 1-bromo-3-acetoxymethyl-2,2-dimethyl-4-methylenecyclohexane (**21**) in the ratio of 2:1.

6-Bromo-4a,5,6,7,8,8a-hexahydro-2,5,5,8a-tetramethyl-4*H*-1-benzopyran (23). A three-neck, 250-ml, round-bottom flask was equipped with a magnetic stirrer and a low-temperature thermometer. The apparatus was flushed with argon and a solution of silver tetrafluoroborate (10 g, 51 mmol) in anhydrous nitromethane was placed in the flask under argon. The solution was cooled to 0° and bromine (51 ml, 1 M Br_2 in CH_3NO_2, 51 mmol) was added dropwise with stirring. The resulting orange complex was then transferred under argon to an addition funnel. A solution of geranylacetone[17] (10.0 g, 51 mmol) in nitromethane was cooled to 0°, and the bromine–silver fluoroborate solution was added dropwise, with rapid stirring. The mixture was stirred for 20 min, then worked up by the addition of saturated sodium bicarbonate solution (100 ml) and extraction with ethyl ether. The ether phase was washed several times with brine solution and dried over anhydrous sodium sulfate. The solvent was removed under high vacuum (approximately 1 mm) at 30°. This left a clear yellow oil (14.9 g of crude material). Thin layer chromatography (TLC) on silica gel (50% ethyl ether–petroleum ether) showed two major spots. The oil was quickly filtered through a short Florisil column (6 × 2 in.). This oil was then submitted to a careful silica gel chromatography using a hexane–ethyl ether gradient. This enabled the isolation of two fractions, A and B, which corresponded to the two spots on the TLC. Fraction A (4.63 g) was the less polar material (R_f 0.5 in petroleum ether). GLC analysis on 6 ft × 2 mm glass column packed with 3% SP2401 on Chromosorb W showed several compounds. Fraction A was rechromatographed on silica gel with hexane to yield the desired cyclic vinyl ether **23:** yield 2.87 g (20%) of a clear pale-yellow oil; ir (CCl_4) 1660, 1375, 1140, 869 cm^{-1}; NMR (220 MHz, CCl_4) δ 0.92 (s, 3 H), 1.05 (s, 3 H), 1.16 (s, 3 H), 1.65 (s, 3 H), 1.82–2.27 (m, 7 H), 4.00 (dd, J = 12,4 Hz, 1 H), 4.47 (t, broad, 1 H); mass spectrum *m/e* (rel abundance) 274, 272 (M^+, 4), 256 (1), 193, 175 (15), 159 (13), 135 (44), 123 (73), 107 (100), 81 (73), 71 (89); high-resolution mass spectrum M^+ 272.0775 ($C_{13}H_{21}O^{79}Br$ requires 272.0776).

4-(5′-Bromo-2′,6′,6′-trimethyl-1′-cyclohexen-1′-yl)-2-butanone (24). Purified bromovinyl ether **23** (100 mg, 0.36 mmol) was dissolved in anhydrous benzene (26 ml). A crystal of recrystallized *p*-toluenesulfonic acid monohydrate was added and the solution was refluxed at 80° for 2 hr. Thin layer chromatography on silica gel (5% ethyl ether–petroleum ether) showed only one spot (R_f 0.5). The reaction mixture was cooled and benzene (10 ml) was added. The solution was carefully washed with sodium bicarbonate solution (2 × 50 ml) and the benzene layer was separated and dried over anhydrous magnesium sulfate. Removal of the solvent left a yellow oil (90 mg). Preparative thick layer chromatography of this oil on silica gel with 20% ethyl–petroleum ether as eluent yielded the desired 4-(5′-bromo-2′,6′,6′-trimethyl-1′-cyclohexen-1′-yl)-2-butanone: yield 70 mg (70%); ir (CCl_4) 1725 cm^{-1}; NMR (220 MHz, CCl_4) δ 1.11 (s, 6 H), 1.54 (s, 3 H), 2.03 (s, 3 H), 4.06 (dd, J = 10, 4 Hz, 1 H); mass spectrum (70 eV) *m/e* (rel abundance) 274, 272 (M^+, 1), 1.93 ($M - Br^+$, 2), 175 ($M - C_2H_4Br^+$, 4), 159 (4), 43 (100).

5-(5′-Bromo-2′,6′,6′-trimethyl-1′-cyclohexen-1′-yl)-3-hydroxy-3-methyl-1-pentene (25). Magnesium turnings (48 mg, 2 mg-atoms) were placed in a three-neck, round-bottom, 100-ml flask equipped with a dry ice condenser, a low-temperature thermometer, a serum cap, and a magnetic stirrer. The apparatus was set up and dried with a heat gun under an argon atmosphere. After the equipment was cool, anhydrous tetrahydrofuran (5 ml) was added and vinyl bromide (107 mg, 1 mmol) was quickly added through a syringe. The reaction mixture was stirred rapidly until all magnesium shavings had dissolved. The temperature was main-

tained below 35° throughout the reaction. The resulting brown solution was diluted with tetrahydrofuran (10 ml) and cooled to 0° in an ice bath. A tetrahydrofuran solution of the methyl ketone **24** (152 mg, 0.56 mmol) was added dropwise with stirring. The mixture was stirred for 15 min at 0°, and then saturated ammonium chloride solution (25 ml) was added slowly. The mixture was extracted with ethyl ether (2 × 25 ml). The ether phase was washed with saturated sodium chloride solution and dried over anhydrous magnesium sulfate. Removal of the solvent left a yellow oil, which was immediately chromatographed on a thick layer silica gel plate, using 20% ether–petroleum ether as eluent (R_f 0.20). This gave 5-(5′-bromo-2′,6′,6′-trimethyl-1′-cyclohexen-1′-yl)-3-hydroxy-3-methyl-1-pentene: yield 154 mg (91%); ir ($CDCl_3$) 3550 sharp, 3420 broad, 1648, 1220, 910 cm^{-1}; NMR (220 MHz, CCl_4) δ 1.19 (s, 6 H), 1.30 (s, 3 H), 1.60 (s, 3 H), 4.22 (dd, J = 10, 4 Hz, 1 H), 5.02 (d, J = 11 Hz, 1 H), 5.18 (d, J = 18 Hz, 1 H), 5.85 (dd, J = 18, 11 Hz, 1 H); mass spectrum m/e (rel abundance) 302, 300 1:1 (M^+, 1.0) 284, 282 1:1 (2.0), 203 (10), 119 (100), 93 (83), 71 (89), 43 (89); high-resolution mass spectrum M^+ 300.1088 ($C_{15}H_{25}O^{79}Br$ requires 300.1089).

10-Bromo-α-chamigrene (1). The alcohol **25** (51 mg, 0.17 mmol) was dissolved in anhydrous benzene (10 ml). A few crystals of *p*-toluenesulfonic acid monohydrate were added and the mixture was heated to reflux for 15 min. Thin layer chromatography after this time showed no starting alcohol. The mixture was cooled and poured over saturated sodium carbonate (25 ml), then washed with saturated sodium chloride. The benzene layer was separated and dried over anhydrous magnesium sulfate. Most of the solvent was removed, and the black residue was put on a short silica gel column. Elution with ethyl ether gave 39 mg of a yellow oil. This material was purified by preparative thick layer chromatography on silica gel with hexane as an eluent to give a clear oil. The GLC on 3% SP2401 showed four components. The major component, with a retention time of 8.5 min, was 10-bromo-α-chamigrene, yield 26.5% (by GLC). The gas chromatograph–mass spectrum of this material was identical in every respect with that of another sample of 10-bromo-α-chamigrene prepared by an independent synthesis. Mass spectrum m/e (rel abundance) 284, 282 1:1 (M^+, 5.9) 216 (53), 214 (55), 203 (17), 202 (39), 187 (13), 173 (5.9), 161 (2.6), 159 (37.6), 147 (27), 145 (21), 135 (100), 119 (85), 105 (46), 91 (39), 81 (20), 79 (19), 77 (21), 69 (12), 67 (12), 45 (18), 43 (11); NMR (220 MHz, CCl_4) δ 0.95 (s, 3 H), 1.08 (s, 3 H), 1.65 (s, 6 H), 4.61 (dd, J = 4, 10 Hz, 1 H), 5.13 (broad, 1 H), 5.31 (broad, 1 H).

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Nucleosides. XXXI.[1] Synthesis of 1-(2,6-Dideoxy-β-D-*arabino*-hexopyranosyl)cytosine, the Nucleoside Portion of Oxamicetin

Frieder W. Lichtenthaler* and Tadeusz Kulikowski[2]

Institut für Organische Chemie, Technische Hochschule Darmstadt, 61 Darmstadt, Germany

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A synthesis of the nucleoside moiety of oxamicetin, 1-(2,6-dideoxy-β-D-*arabino*-hexosyl)cytosine (**3**), is described starting from the known 1-(2-deoxy-β-D-*arabino*-hexosyl)uracil (**7**). The synthetic sequence involved selective mesylation at the primary hydroxyl group, displacement by iodide, and reductive dehalogenation (**7** → **8** → **9** → **10**) followed by conversion of uracil nucleoside **10** into its cytosine analogue **3** by O-benzoylation, thiation, and ammonolysis. Structural and configurational assignments evolved from the mode of preparation as well as from spectroscopic data, a consideration of the circular dichroism Cotton effects indicating that the sugar-base conformation is strongly dependent on the nature of the 6′ substituent.

Oxamicetin (**1**), a new disaccharide nucleoside antibiotic isolated recently from the fermentation broth of *Arthrobacter oxamicetus*,[3,4] has been allotted[5] to the aminoacyl-4-aminohexosylcytosine group of protein biosynthesis inhibitors[6] on the basis of a close similarity to amicetin (**2**) in its gross antibacterial activity,[4] its inhibitory effect on the fragment reaction,[5] and its structural features,[7] differing from **2** only by an additional hydroxyl group in the disaccharide unit. The structural assignments within the nucleoside portion were mainly based on the isolation of 1-(2,6-dideoxy-β-D-*arabino*-hexopyranosyl)cytosine (**3**) on acid methanolysis, for which the alternate β-L-arabino configuration was excluded via the copper complex method.[7] This paper provides confirmatory evidence for the β-D-arabino configuration by an unequivocal synthesis of the nucleoside portion **3** and the proof of its identity with the oxamicetin derived product.

Of the several approaches conceivable for the synthesis of **3**, the utilization of the pyrimidinone nucleoside **4**, accessible from 3,4,6-tri-*O*-nitrobenzoyl-2-deoxy-α-D-*arabino*-hexosyl bromide and 2,4-diethoxypyrimidine in a remarkably stereoselective reaction,[8] was considered more propi-