# The Structure of Notoryne, a Halogenated $C_{15}$ Nonterpenoid with a Novel Carbon Skeleton from the Red Alga *Laurencia nipponica* Yamada[1)]

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A new halogenated $C_{15}$ nonterpenoid with a novel carbon framework, named notoryne, has been isolated from the title alga and its structure was established on the basis of spectroscopic and chemical evidence. In addition, the structure of a rearranged product, whose structure has long remained unsettled, of laurefucin derivative was also determined by spectral and chemical methods. Furthermore, the biogenesis of the halogenated $C_{15}$ nonterpenoids from *L. nipponica* collected at warm current region in Hokkaido is also discussed.

Red algae of the genus *Laurencia* are known to produce halogenated $C_{15}$ nonterpenoid ethers containing different ring systems, which usually have a conjugated enyne or a bromoallene moiety at one end of the molecule.[2,3)] Among the Japanese species of the genus *Laurencia, L. nipponica* displayed a marked variation in the major metabolites, which seems to be mainly dependent upon the growth locality. The major metabolites from this species, collected in the warm current region in Hokkaido, are, with some exception,[4,5)]

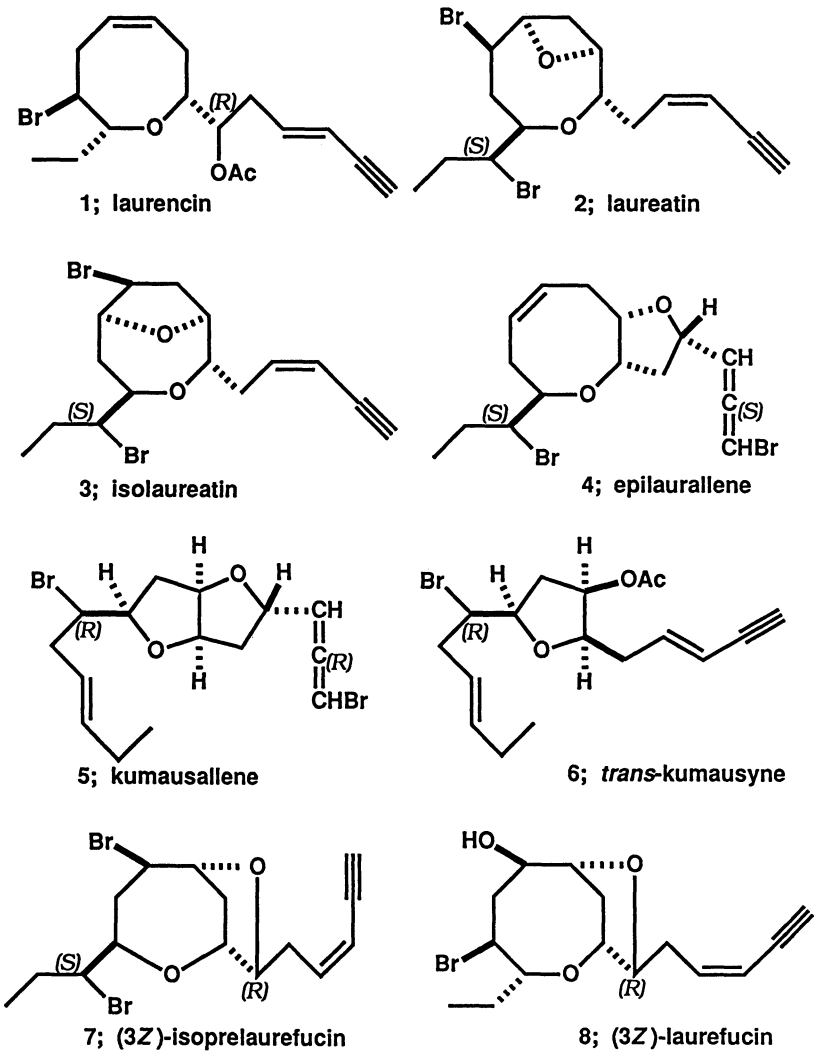


Fig. 1. The main $C_{15}$ nonterpenoids from *Laurencia nipponica* collected in the warm current region in Hokkaido.

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composed of $C_{15}$ nonterpenoids, e.g. laurencin (**1**),[6,15] laureatin (**2**),[7,9,15] isolaureatin (**3**),[8,9,15] epilaurallene (**4**),[10,15] kumausallene (**5**),[11,13] *trans*-kumausyne (**6**),[12,13] and (3*Z*)-isoprelaurefucin (**7**)[14] (Fig. 1).

In connection with our studies on this species growing in the warm current region in Hokkaido, we have newly made collection at Notoro Point, near Abashiri, and examined its constituents. This specimen contained (3*Z*)-laurefucin (**8**)[16] as the major metabolite and a new $C_{15}$ nonterpenoid, which we have named notoryne, as a minor one. In this paper we report the isolation and the structure elucidation of notoryne (**9**) as well as the structure of a rearranged product **22**, which has previously been obtained from laurefucin derivative.[17] Furthermore, the biogenesis of $C_{15}$ nonterpenoids from *Laurencia nipponica* collected at warm current region in Hokkaido is also discussed.

Notoryne (**9**), colorless oil, $[\alpha]_D$ +40.3° ($CHCl_3$), had a molecular formula of $C_{15}H_{20}BrClO_2$. The presence of a (*Z*)-2-penten-4-ynyl side chain in **9** was evident from the UV [$\lambda_{max}$ 223 nm ($\varepsilon$ 12500)], IR [$\nu_{max}$ 3300 and 2100 $cm^{-1}$], $^1H$ NMR [$\delta$=3.13 (1H, dd, *J*=2.4 and 0.8 Hz), 5.60 (1H, dddd, *J*=10.3, 2.4, 1.3, and 1.3 Hz), and 6.08 (1H, dddd, *J*=10.8, 7.3, 7.3, and 0.8 Hz)], and mass [*m/z* 285, 283, and 281 ($M^+-C_5H_5$)] spectra. Furthermore, the $^1H$ NMR spectrum revealed the presence of a methyl group at $\delta$=1.00 (3H, dd, *J*=7.3 and 7.3 Hz) and six methine groups at $\delta$=3.88 (1H, ddd, *J*=8.3, 7.3, and 6.8 Hz), 3.91 (1H, ddd, *J*=7.3, 7.2, and 3.9 Hz), 3.98 (1H, ddd, *J*=8.3, 6.8, and 5.5 Hz), ca. 4.1 (2H, m), and 4.26 (1H, ddd, *J*=7.3, 7.3, and 5.5 Hz) which are flanked by a bromine, a chlorine, or an oxygen atom. Since the IR spectrum of **9** showed no hydroxyl and carbonyl absorptions, both oxygen atoms in **9** were assumed to be involved in ether links. Moreover, the $^{13}C$ NMR spectrum of **9** showed no other double bonds other than those of the conjugated enyne moiety, and hence **9** must be composed of two oxide rings.

Extensive spin decoupling experiments in the $^1H$ NMR spectrum of **9** indicated the presence of the following partial structure (Fig. 2) for **9**. Hydrogenation of **9** with platinum oxide in ethanol gave a hexahydro derivative **10**, $C_{15}H_{26}BrClO_2$. The $^1H$ NMR spectrum of **10** displayed no signals at $\delta$=3.5—2.9 due to epoxide protons[18] and at near $\delta$=2.7 due to methylene protons on a 1,3-disubstituted oxetane ring.[9,19] Furthermore, the mass spectrum of **10** showed no fragment ions due to a 1-halopropyl or a 1-halohexyl moiety, thus suggesting that the substituents at C-6 and C-13 must not be halogen atoms but oxygen atoms.

The FI mass spectrum of **9** showed significant fragment ions at *m/z* 285, 283, 281 (32:100:80), 179, 177 (45:45), and 171, 169 (3:10). On the other hand, the EI mass spectrum of **9** showed a base peak at *m/z* 133 and significant peaks at *m/z* 97 and 69 along with those at *m/z* 285, 283, 281, 179, and 177. The main fragmentation in both spectra would be explicable as shown in Scheme 1, leading to formula **9** as the most favor-

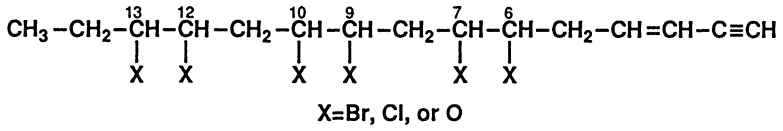
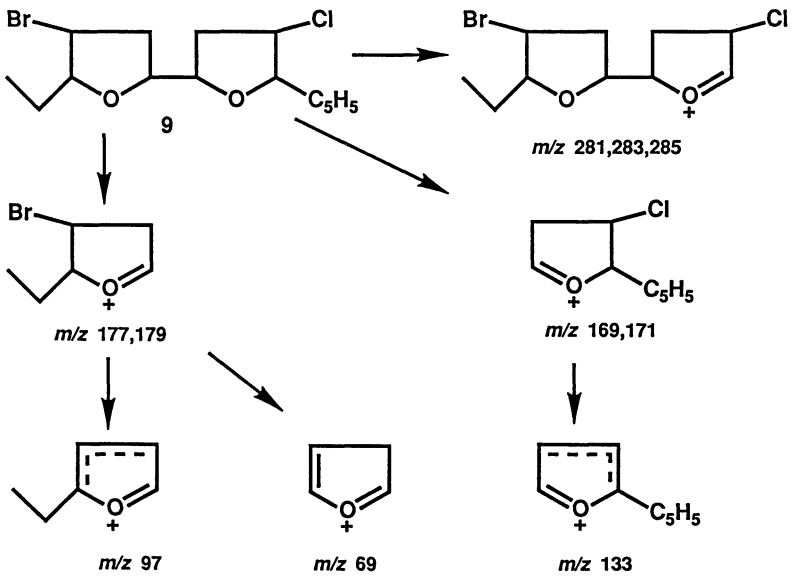
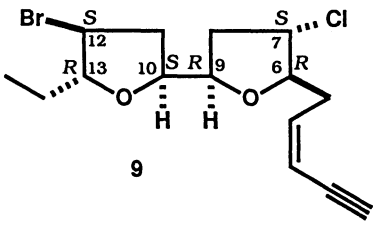



Fig. 2. Partial structure for notoryne (**9**).




Scheme 1. The main fragmentation in the mass spectra of **9**.



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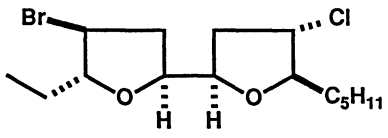

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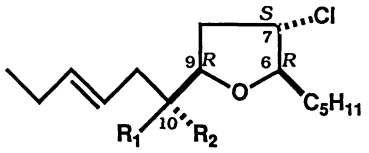
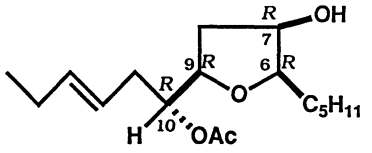


11; $R_1$=OH, $R_2$=H
14; $R_1$=H, $R_2$=OAc
15; $R_1$=H, $R_2$=OH
16; $R_1$=$R_2$=O
17; $R_1$=H, $R_2$=Br
18; $R_1$=Br, $R_2$=H



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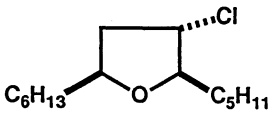

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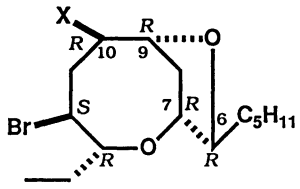
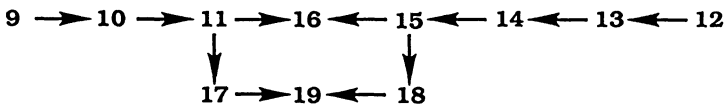


12; X=OAc
20; X=Br
21; X=OH
39; X=Cl



Scheme 2. Chemical correlation of **9**.

able planar structure for notoryne. Confirmation of the structure was obtained by the following chemical correlation with known compound (Scheme 2).

Treatment of **10** with zinc and acetic acid in methanol gave a chloro alcohol **11**, $C_{15}H_{27}ClO_2$, $\nu_{max}$ 3550, 3430, 3030, and 970 $cm^{-1}$. The $^1H$ NMR spectrum of **11** revealed signals due to a *trans* double bond at $\delta$=5.34 and 5.62 (each 1H, dt, $J$=15 and 6 Hz). The mass spectrum of **11** showed fragment ions at $m/z$ 207, 205 (3:9; $M^+-C_5H_{11}$) and 177, 175 (4:14; $M^+-C_6H_{11}O$), suggesting **11** possesses an oxolane ring containing a chlorine atom, a $C_5$-side chain, and a $C_6$-side chain with a hydroxyl group.

On the other hand, the acetoxy alcohol **13**,[17,20] which was obtained by treatment of hexahydroacetyllaurefucin (**12**)[17,20] with zinc and acetic acid in methanol, was treated with carbon tetrachloride and triphenylphosphine in benzene to give a chloro acetate **14**, $C_{17}H_{29}ClO_3$, whose IR spectrum showed no hydroxyl absorption. This halogenation reaction with carbon tetrahalide and triphenylphosphine usually proceeds in the $S_N2$ manner with inversion of configuration.[21] Therefore, the configuration at C-7 in **13** must have been inverted from *R* to *S*. Saponification of **14** with potassium carbonate in methanol yielded the corresponding chloro alcohol **15**, $C_{15}H_{27}ClO_2$, whose spectral data showed a close resemblance to those of the chloro alcohol **11** derived from **9**. Collins oxidation of both the chloro alcohols, **11** and **15**, gave the same ketone **16**, $C_{15}H_{25}ClO_2$, thus indicating that the both chloro alcohols are an epimer of the hydroxyl group at C-10. This was confirmed by the following reactions.

On treatment with carbon tetrabromide and triphenylphosphine in benzene, a chloro alcohol **11** gave a bromochloro ether **17**, $C_{15}H_{26}BrClO$. On the other hand, another chloro alcohol **15** also gave a bromochloro ether **18** on bromination with carbon tetrabromide and triphenylphosphine. Both the halo ethers **17** and **18** afforded the same tetrahydrofuran derivative **19**, $C_{15}H_{29}ClO$, by Raney nickel reduction in ethanol, thus proving that the chiral centers at C-6, C-7, C-9, and C-10 of the chloro alcohol **11** should be represented by *R*-, *S*-, *R*-, and *S*-configuration, respectively. Thus the structure of notoryne can be assigned as formula **9** except for the configurations at C-12 and C-13, which are discussed later.

Previously Fukuzawa et al.[17] have observed that a dibromo compound **20**, which was obtained by the bromination of hexahydrolaurefucin (**21**) with thionyl bromide in ether, is converted into a rearranged product

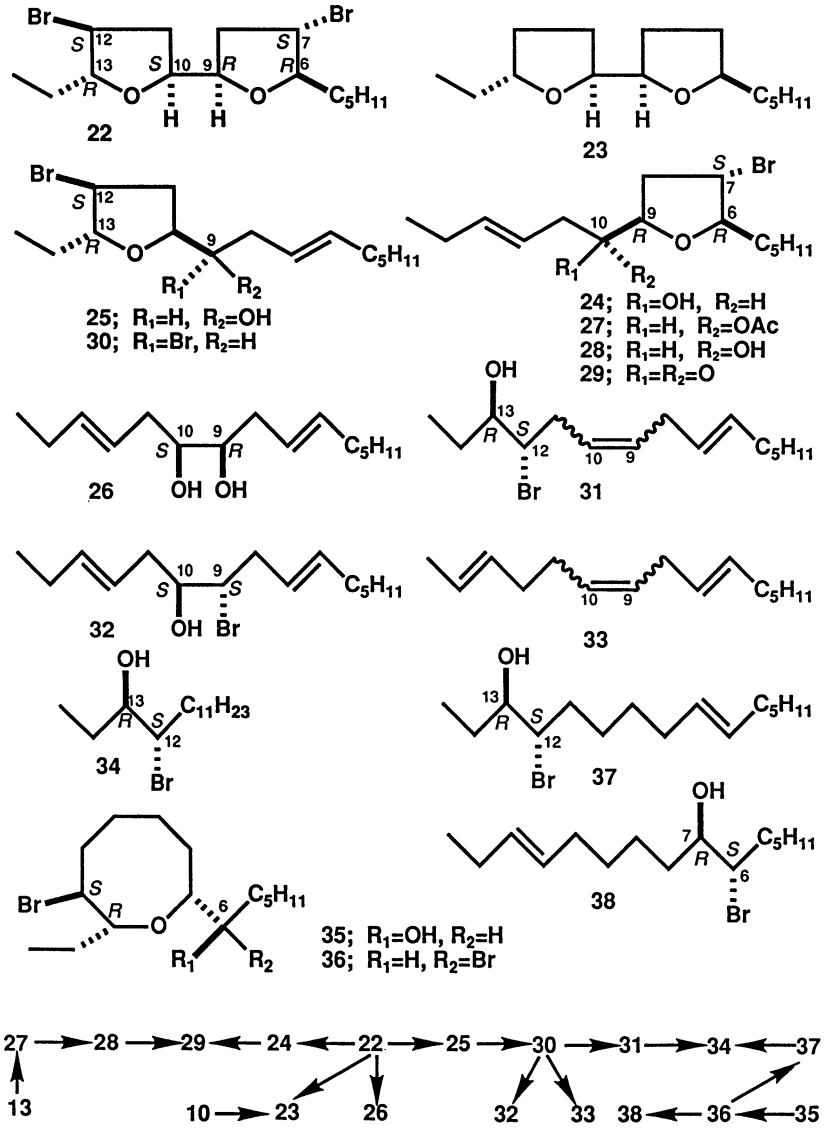
**22**, which has the same molecular formula of $C_{15}H_{26}Br_2O_2$ as that of **20**, on silica-gel column chromatography. The structure of this rearranged product **22** has long remained unresolved.

The spectral properties of **22** were very similar to those of hexahydronotoryne (**10**), suggesting that **22** possesses the same carbon skeleton, including an ethyl group, a pentyl group, and two bromine atoms, as that of **10**. This was confirmed by the following chemical derivation (Scheme 3).

Treatment of **10** with Raney nickel in refluxing ethanol gave a dehalogenated compound **23**, $C_{15}H_{28}O_2$. On the other hand, the rearranged product **22** was also treated with Raney nickel in ethanol at room temperature to afford a debrominated compound which was found to be identical with **23** in all respects. Above results indicated that the rearranged product **22** possesses the same stereochemistry at C-6, C-9, C-10, and C-13 as that of **10**. The locations of two bromine atoms and their stereochemistry as well as that at C-12 and C-13 were determined as follows.

Treatment of **22** with zinc and acetic acid in methanol gave two unsaturated bromo alcohols, **24** and **25**, which have the same molecular formula of $C_{15}H_{27}BrO_2$, and a glycol **26**[17,20] in 25, 49, and 16% yields, respectively. One of the bromo alcohols, compound **24** showed in its $^1H$ NMR spectrum the presence of two methyl groups, four methine groups, and a *trans* double bond. The mass spectrum of **24** exhibited significant fragment ions at 221, 219 ($M^+-C_6H_{11}O$) and 99 ($M^+-C_9H_{16}BrO$), arising from the $C_9$–$C_{10}$ single bond cleavage. As shown in Scheme 3, the assigned structure **24** was confirmed by the correlation with the acetoxy alcohol **13** as in the case of compound **11** derived from hexahydronotoryne (**10**). Collins oxidation of **24** gave a bromo ketone **29**, which was identical with the ketone derived from **13** via a bromo acetate **27** and a bromo alcohol **28**.

Another bromo alcohol **25** also showed in its




Scheme 3. Chemical correlation of the rearranged product **22**.

$^1$H NMR spectrum the presence of two methyl groups, four methine groups, and a *trans* double bond. The mass spectrum of **25** showed significant fragment ions at 179, 177 ($M^+-C_9H_{17}O$) and 141 ($M^+-C_6H_{10}BrO$), which should also be generated by $C_9$–$C_{10}$ bond cleavage. These data are consistent with the assigned structure **25**, except for the configurations at C-12 and C-13. The absolute configurations at C-12 and C-13 in **25** were established by the chemical correlation to laurencin (**1**).

Treatment of **25** with carbon tetrabromide and triphenylphosphine in benzene afforded a dibromo compound **30**, $C_{15}H_{26}Br_2O$, which was then treated with zinc and acetic acid in methanol to give three products, two of which were unsaturated bromohydrins **31** and **32**, $C_{15}H_{27}BrO$. Another reduction product was an unsaturated hydrocarbon **33**, $C_{15}H_{26}$. One of the unsaturated bromohydrins, compound **31**, which was found to be a mixture of (9*Z*)- and (9*E*)-isomer (ca. 2:3) by the $^1$H NMR (400 MHz) spectrum, was hydrogenated with $PtO_2$ in ethanol to yield a saturated bromohydrin **34**, $C_{15}H_{31}BrO$.

On the other hand, octahydrodeacetyllaurencin (**35**)[6] was treated with carbon tetrabromide and triphenylphosphine in benzene to give a dibromide **36**, $C_{15}H_{28}Br_2O$,[22] which was then subjected to the reduction with zinc and acetic acid in methanol to afford two unsaturated bromohydrins **37** and **38**, $C_{15}H_{29}BrO$. One of the bromohydrins, compound **37** was subsequently hydrogenated with $PtO_2$ in ethanol to yield a saturated bromohydrin which was identical with the bromohydrin **34** in all respects, thus indicating that the absolute configurations at C-12 and C-13 in compound **25** are assigned as *S* and *R*, respectively. Therefore, it is concluded that the structure of the rearranged product must be represented by formula **22**, including the absolute configuration.

As already mentioned above, the configuration at C-13 of hexahydronotoryne (**10**) is the same as that of the rearranged product **22**, and hence the absolute configuration at C-13 of **10** is also assigned as *R*. The configuration at C-12 of **10** was deduced from the following evidence. In the 400 MHz $^1$H NMR spectra, the signals due to the methine protons at C-12 in compounds **10** and **22** revealed the same chemical shift and splitting pattern at $\delta$=3.86 (ddd, $J$=8.3, 7.3, and 6.8 Hz). Furthermore, compound **22**, on treatment with zinc and acetic acid in methanol, gave (12*E*)-olefin **24** as a sole product. Similarly, hexahydronotoryne (**10**) also afforded only (12*E*)-olefin **11** under the same reduction conditions as in the case of **22**. Since the degradation proceeds through E2 mechanism under *trans*-periplanar arrangement of the bromine atom at C-12 and the ethereal oxygen atom at C-13, the (12*E*)-double bond in **11** and **24** should arise from *erythro* configuration between C-12 and C-13. These findings strongly indicated that the absolute configuration at C-12 of hexahydronotoryne (**10**) is *S*, the same as that of **22**.

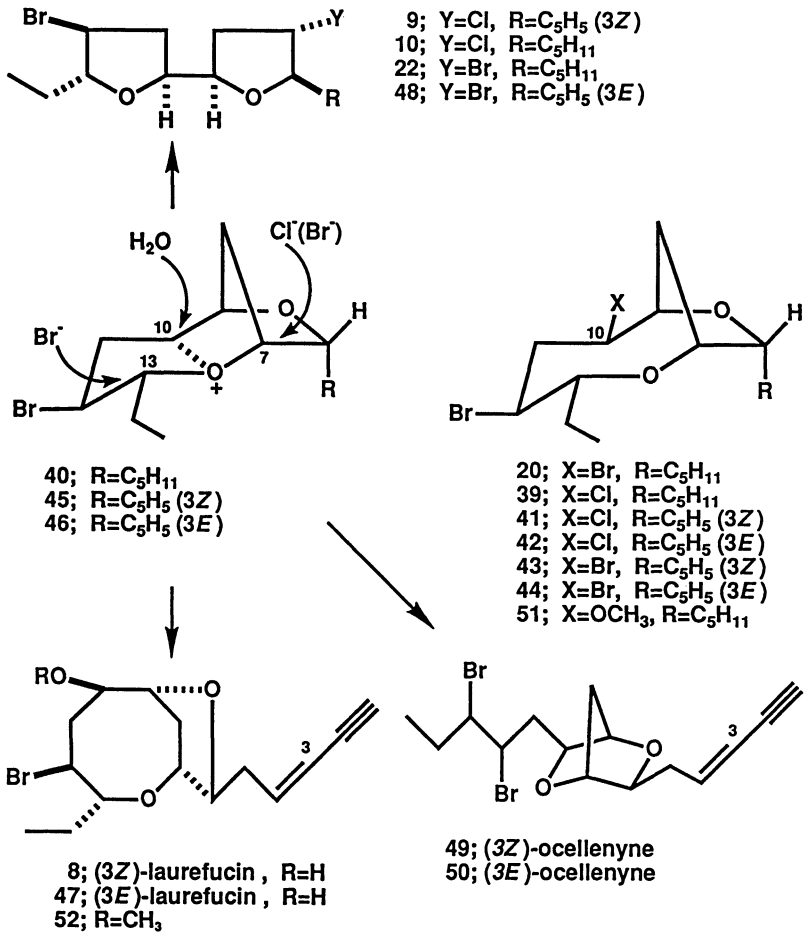
Accordingly, the structure of notoryne, including the absolute configuration, must be shown as formula **9**.

The structural similarity between hexahydronotoryne (**10**) and the rearranged product **22** suggested that a chloro compound **39**, when treated with silica gel, would give hexahydronotoryne (**10**). As anticipated, the chloro compound **39**, prepared from hexahydrolaurefucin (**21**) by chlorination with thionyl chloride in ether, afforded hexahydronotoryne (**10**) in quantitative yield when it was treated with activated silica gel[23] in hexane at room temperature for 24 h. Furthermore, on treatment with aluminum oxide (Merck, activity II-III) or silica gel (Merck, Kieselgel 60), the chloro compound **39** gave hexahydronotoryne (**10**) and hexahydrolaurefucin (**21**) in about 20 and 80% yields, respectively. On the other hand, on treatment with activated silica gel, the dibromo compound **20** gave the rearranged product **22** in almost quantitative yield. Moreover, compound **20** afforded hexahydrolaurefucin (**21**) in quantitative yield on treatment of aluminum oxide and also afforded **22** and **21** in 40 and 60% yields on treatment with silica gel.

The mechanism of the rearrangement reactions of compounds **20** and **39** would be explained by assuming that an oxonium ion may serve as an intermediate as shown in Scheme 4.

The stereochemistry of the bromine atom at C-10 of the dibromo compound **20** was unambiguously established as a $\beta$-oriented configuration by X-ray crystallographic analysis.[24] Since the close resemblance of the chemical shifts and multiplicities in the 400 MHz $^1$H NMR spectra of **20** and **39** indicated that the configurations at C-10 and the ring conformations in **20** and **39** are nearly identical, the configuration at C-10 in **39** must be *R*. In **20** and **39**, the 2p orbital of the lone pair on the oxygen atom of the oxocane ring is situated close to the C–X (X=Br or Cl) bond at C-10 (about 2.81 Å in the crystalline state), the formation of an oxonium ion **40** can be rationalized by transannular participation of the ether oxygen. Reactions of the resulting oxonium ion **40** with bromide ion or chloride ion at C-7 position would lead to the rearranged product **22** or hexahydronotoryne (**10**), respectively. Furthermore, reaction of cation **40** with water at C-10 position would lead to hexahydrolaurefucin (**21**).

The isomerization reactions described above suggested that notoryne (**9**) could be an artifact generated during the course of the isolation procedure, in which aluminum oxide and silica gel have been used as the absorbent for chromatography. Thus the separation was carried out with high performance liquid chromatography (Finepak SIL-$C_{18}$ with $CH_3CN$–$H_2O$ (70:30)), under whose condition the synthetic **41**, prepared from (3*Z*)-laurefucin (**8**) by chlorination with thionyl chloride in ether, was unchanged. The HPLC of the neutral oil gave notoryne (**9**) and (3*Z*)-laurefucin (**8**) in ca. 5 and 18% yields, respectively. However, compound **41** could not be detected. Furthermore, the possibility that **9** was produced during the extraction procedure can be ruled out on the basis of the following evidence. Both



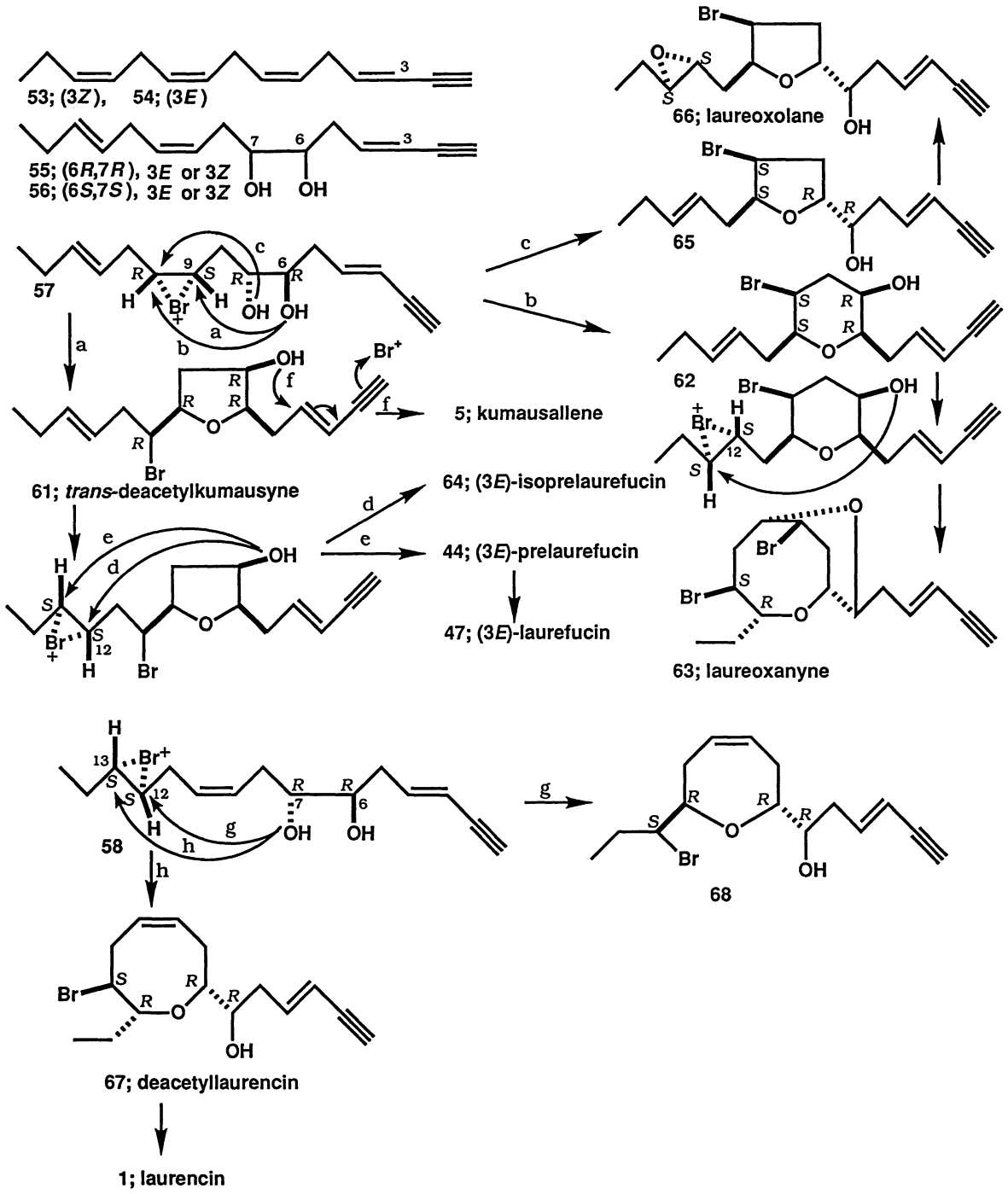

Scheme 4. Mechanism of the rearrangement reaction.

the compounds **20** and **39**, when treated with aqueous methanol, gave an *O*-methyl derivative which was identical with *O*-methylhexahydrolaurefucin (**51**) derived by hydrogenation from *O*-methyllaurefucin (**52**),[25] which has been isolated from the methanol extracts of *Laurencia nipponica* collected at several locations and must be an artifact formed during the extraction procedure. However, the neutral methanol extract of Notoro's specimen displayed the absence of *O*-methyllaurefucin (**52**). These results strongly indicate that notoryne (**9**) is a natural product.

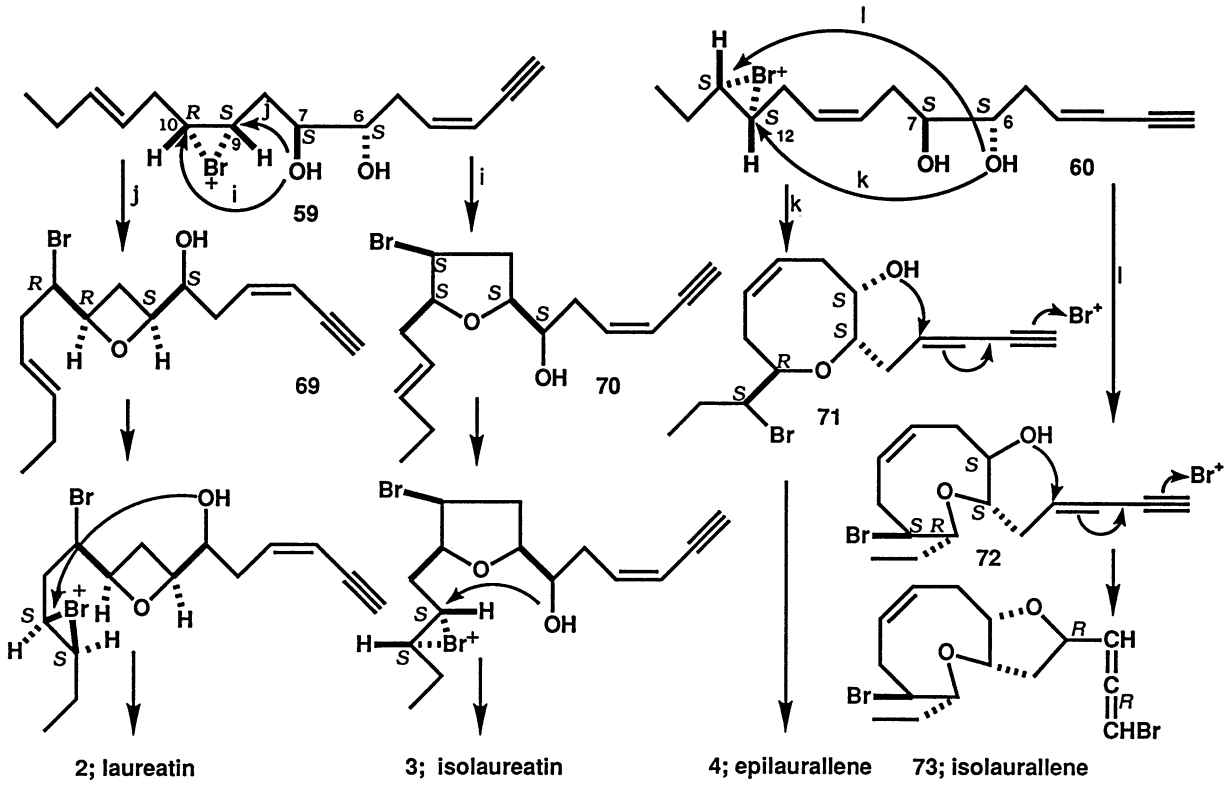
As shown in Scheme 4, notoryne (**9**) would be enzymatically synthesized from compound **41**, designated as (3*Z*)-neoprelaurefucin, via the oxonium ion **45** by attack of chloride ion at C-7. (3*Z*)-Neoprelaurefucin (**41**) and (3*E*)-neoprelaurefucin (**42**) may serve as the precursors of (3*Z*)-laurefucin (**8**) and (3*E*)-laurefucin (**47**), formed via cations **45** and **46** by attack of water at C-10, respectively. Furthermore, compounds **43** and **44**, designated as (3*Z*)-prelaurefucin and (3*E*)-prelaurefucin, could serve also as the precursors of **8** and **47**. *O*-Methyllaurefucin (**52**) (3*E*) would be formed via the oxonium ion **46** by attack of methanol at C-10. Both neoprelaurefucins, **41** and **42**, and prelaurefucins, **43** and **44**, phantasmal metabolites, have not been isolated from natural sources. On the other hand, (3*E*)-prelaurefucin (**44**) would give a dibromide **48**, which has not yet been isolated so far, via the cation **46** by attack of bromide ion at C-7 as in the case of notoryne (**9**). More recently, lauroxolane, which has the same molecular formula and the same carbon skeleton as those of **48**, has been isolated from *Laurencia majuscula* collected off the North Shore of Oahu, Hawaii.[26] A comparison of the spectral data of lauroxolane and those of the rearranged product **22** indicates that the relative stereochemistry of lauroxolane must be different from that of **22**. Furthermore, (3*Z*)-prelaurefucin (**43**) and (3*E*)-prelaurefucin (**44**) also seem to serve as the precursors of (3*Z*)- and (3*E*)-ocellenyne, **49** and **50**, which have previously been isolated from the sea hare *Aplysia oculifera*.[27] Ocellenynes would be formed via the oxonium ion **45** and **46** by attack of bromide ion at C-13.

The $C_{15}$ nonterpenoids isolated from *L. nipponica*, whose major representatives are shown in Fig. 1, may be derived from laurencenyne (**53**)[28,30] or *trans*-laurencenyne (**54**)[29,30,5] via (6*R*,7*R*)- or (6*S*,7*S*)-laurediols, **55** (3*E* or 3*Z*) and **56** (3*E* or 3*Z*),[31] which have also been isolated from the same alga. As illustrated in Schemes 5 and 6, the formation of cyclic ethers with various ring size can be rationalized by the cyclization of the

(9*S*,10*R*)-bromonium ions, **57** and **59**, or (12*S*,13*S*)-bromonium ions, **58** and **60**, derived from laurediols. These bromonium ions may arise from laurediols by the addition of $Br^+$ generated from $Br^-$ by bromoperoxidase[32,33] to the double bonds at C-9 or C-12. Reaction of the bromonium ion **57** (3*E*) (Scheme 5) with the hydroxyl group at C-6 would lead to the bromo ethers **61** and **62**. The former bromo ether **61** is *trans*-deacetylkumausyne.[12] The latter bromo ether **62**, which has not yet been found so far, may give laureoxanyne (**63**)[34] via (12*S*,13*S*)-bromonium ion. *trans*-Deacetylkumausyne (**61**) may further afford (3*E*)-prelaurefucin (**44**) and (3*E*)-isoprelaurefucin (**64**)[35,14] also via (12*S*,13*S*)-bromonium ion. Kumausallene (**5**) may also arise from *trans*-deacetylkumausyne (**61**) by bromonium ion-catalyzed cyclization. Furthermore, reaction of the bromonium ion **57** with the hydroxyl group at C-7 would give the bromo ether **65**, which must afford laureoxolane (**66**),[36] isolated from this alga as a minor component. Reaction of the bromonium ion **58** (3*E*) with the hydroxyl group at C-7 would lead to the formation of deacetyllaurencin (**67**)[6] and deacetyliso-




Scheme 5. Biogenesis from (6*R*,7*R*)-laurediols.




Scheme 6. Biogenesis from (6*S*,7*S*)-laurediols.

laurencin (**68**).[37]

On the other hand, on reaction with the hydroxyl group at C-7, the bromonium ion **59** (3*Z*) (Scheme 6) would give the bromo ethers **69** and **70**, from which laureatin (**2**)[7,9] and isolaureatin (**3**)[8,9] may be derived also via (12*S*,13*S*)-bromonium ions, respectively. Furthermore, reaction of the bromonium ion **60** with the hydroxyl group at C-6 would give two bromo ethers **71** and **72**. Epilaurallene (**4**)[10] or laurallene[38] may arise from the bromo ether **71** by bromonium ion-catalyzed cyclization. Similarly, the bromo ether **72** may give isolaurallene (**73**),[39] which has been isolated from this alga as a minor component.

## Experimental

All the melting points were uncorrected. The IR spectra were measured on a JASCO A-102 spectrophotometer and the UV spectra on a Hitachi 124 or a Shimadzu UV-240 spectrophotometer. The $^1$H NMR spectra were obtained in $CDCl_3$ as the solvent with TMS as the internal standard by using a JEOL JNM-FX-100, JNM-FX-400, or JNM-PS-100 spectrometer. The $^{13}$C NMR spectra were recorded on a JEOL JNM-FX-100 spectrometer in $CDCl_3$ solution. The low and high resolution EI-MS spectra were measured on a JEOL JMS-D300 spectrometer, and the low FI-MS spectrum was taken with a JEOL JMS-OISG-2 spectrometer. Optical rotations were measured on a JASCO DIP-140 polarimeter in $CHCl_3$ solution. Aluminum oxide (Merck, activity II-III) and silica gel (Merck, Kieselgel 60, 70—230 mesh) were used for column chromatography. The high performance liquid chromatography (HPLC) was performed on a JASCO TRI-ROTAR using Finepak SIL-$C_{18}$ column (JASCO).

**Isolation.** Half-dried alga (8 kg), which was collected at Notoro Point, near Abashiri, Hokkaido, in July 31, 1981, was extracted with MeOH and the neutral MeOH exrtract (59 g) obtained by the conventional methods was fractionated by column chromatography over standard alumina. The fraction eluted with hexane gave a mixture of hydrocarbons, which was repeatedly chromatographed on silica-gel column with hexane to yield isodihydrolaurene (2.5% of the neutral oil),[4] laurene (2.1%),[40] and *trans*-laurencenyne (0.7%).[29] The fraction eluted with benzene were further subjected to repeated column chromatography over silica gel with benzene to give nidificene,[13,41] (3*Z*)-laurediol acetate,[31] and crude notoryne which was purified by silica-gel column chromatography with hexane/benzene (1 : 3) to give pure notoryne (**9**) (5.0%). The fraction eluted with benzene/EtOAc (10 : 1) afforded debromoallolaurinterol (1.0%),[16,42] (3*Z*)-acetyllaurefucin (1.3%),[16] and (3*Z*)-7-acetyllaurediol (2.6%). The fraction eluted with EtOAc was further chromatographed on silica-gel column with benzene–EtOAc (1 : 1) to yield (3*Z*)-laurefucin (18%).[16]

**Notoryne (9):** Colorless oil; $[\alpha]_D$ +40.3° (*c* 1.03); UV (ethanol), $\lambda_{max}$ 223 nm ($\varepsilon$ 12500) and $\lambda_{inf}$ 220 ($\varepsilon$ 10300) and 231 nm ($\varepsilon$ 9400); IR (neat), $\nu_{max}$ 3300, 3030, 2100, 1615, 1110, 1070, 1025, 970, 920, and 735 cm$^{-1}$, $^1$H NMR (400 MHz) $\delta$=1.00 (3H, t, *J*=7.3 Hz, $H_3$-15), 1.49 (1H, dqd, *J*=14.3, 7.3, 7.2 Hz, H-14), 1.76 (dqd, *J*=14.3, 7.3, 3.9 Hz, H-14), 2.17 (1H, ddd, *J*=13.2, 8.3, 8.3 Hz, H-11), 2.3 (2H, m, $H_2$-8), 2.59 (1H, dddd, *J*=14.8, 7.3, 7.0, 1.3 Hz, H-5), 2.66 (1H, ddd, *J*=13.2, 6.8, 6.8 Hz, H-11), 2.67 (1H, m, H-5), 3.13 (1H, dd, *J*=2.4, 0.8 Hz, H-1), 3.88 (1H, ddd, *J*=8.3, 7.3, 6.8 Hz, H-12), 3.91 (1H, ddd,

$J$=7.3, 7.2, 3.9 Hz, H-13), 3.98 (1H, ddd, $J$=8.3, 6.8, 5.5 Hz, H-10), 4.1 (2H, m, H-6 and H-7), 4.26 (1H, ddd, $J$=7.3, 7.3, 5.5 Hz, H-9), 5.60 (1H, dddd, $J$=10.8, 2.4, 1.3, 1.3 Hz, H-3), and 6.08 (1H, dddd, $J$=10.8, 7.3, 7.3, 0.8 Hz, H-4); $^{13}$C NMR (25.0 MHz) $\delta$=10.0 (q, C-15), 25.4 (t, C-14), 34.3 (t, C-5), 38.0 (t, C-11 or C-8), 39.3 (t, C-8 or C-11), 47.2 (d, C-12), 59.1 (d, C-7), 78.8 (d, C-13 or C-6), 79.8 (s, C-2), 79.9 (d, C-6 or C-13), 82.1 (d, C-1), 85.9 (d, C-9 or C-10), 87.0 (d, C-10 or C-9), 110.8 (d, C-3), and 139.5 (d, C-4); EI-MS (70 eV) $m/z$ (rel intensity) 313, 311 (0.3:0.3; $M^+-Cl$), 285, 283, 281 (5:21:16; $M^+-C_5H_5$), 284, 282 (1:1; $M^+-Cl-C_2H_5$), 201 (3; $M^+-HBr-HCl-C_2H_5$), 179, 177 (3:3; $M^+-C_9H_{10}ClO$), 135 (16), 133 (100; $M^+-C_6H_{10}BrO-HCl$), 105 (14), 97 (47; $M^+-C_9H_{10}ClO-HBr$), 69 (36; $M^+-C_9H_{10}ClO-Br-C_2H_5$), 55 (8), and 41 (17); FI-MS (70 eV), $m/z$ 350, 348, 346 (27:63:43; $M^+$), 285, 283, 281 (32:100:84; $M^+-C_5H_5$), 284, 282 (16:16; $M^+-Cl-C_2H_5$), 269, 267 (6:13; $M^+-Br$), 179, 177 (45:45; $M^+-C_9H_{10}ClO$), and 171, 169 (3:10; $M^+-C_6H_{10}BrO$). Found: $m/z$ 282.9923. Calcd for $C_{10}H_{15}{}^{81}Br^{35}ClO_2$: $M-C_5H_5$, 282.9923.

**Hydrogenation of Notoryne (9).** The hydrogenation of **9** (12 mg) was performed in EtOH over $PtO_2$-catalyst to give an oily product which was chromatographed on silica-gel column with hexane–benzene (2:1) to afford hexahydronotoryne (**10**) (12 mg); colorless oil; $[\alpha]_D$ +52.6° ($c$ 0.980); IR (neat), $\nu_{max}$ 1290, 1120, 1100, 1070, 1030, 970, 925, 790, and 740 cm$^{-1}$; $^1$H NMR (400 MHz) $\delta$=0.89 (3H, br t, $J$=6.8 Hz), 1.00 (3H, t, $J$=7.3 Hz), 1.2—1.6 (9H, m), 1.75 (1H, dqd, $J$=15.0, 7.3, 4.4 Hz), 2.13 (1H, ddd, $J$=13.2, 8.3, 8.3 Hz), 2.23 (2H, dd, $J$=7.3, 5.9 Hz), 2.65 (1H, ddd, $J$=13.2, 6.8, 6.8 Hz), 3.86 (1H, ddd, $J$=8.3, 7.3, 6.8 Hz), 3.8—4.0 (4H, m), and 4.22 (1H, ddd, $J$=7.3, 7.3, 5.4 Hz); EI-MS (70 eV), $m/z$ 318, 316 (0.2:0.2; $M^+-HCl$), 274, 272 (0.1:0.3; $M^+-HBr$), 179, 177 (9:9; $M^+-C_9H_{16}ClO$), 177, 175 (8:25; $M^+-C_6H_{10}BrO$), 139 (37; $M^+-HCl-C_6H_{10}BrO$), 121 (12), 97 (100; $M^+-C_9H_{10}ClO-HBr$), 95 (15), 69 (40; $M^+-C_9H_{16}OCl-Br-C_2H_5$), 55 (14), and 41 (23).

**Conversion of Hexahydronotoryne (10) into 11.** To a solution of **10** (20 mg) and AcOH (80 $\mu$l) in MeOH (1 ml) was added activated Zn-dust (150 mg), and the mixture was stirred for 21 h at room temperature under $N_2$ atmosphere. After being filtered off and evaporated, the mixture was extracted with ether. The ethereal solution was washed successively with water, 5% aqueous $NaHCO_3$, and water. After drying over $Na_2SO_4$, the solvent was evaporated to give a residual oil which was purified by column chromatography over silica gel with hexane–benzene (1:3) to yield **11** (15 mg); oil; $[\alpha]_D$ +31.6° ($c$ 0.530); IR (neat), $\nu_{max}$ 3550, 3430, 3030, 1280, 1120, 1065, 1045, 1020, and 970 cm$^{-1}$; $^1$H NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=6 Hz), 0.98 (3H, t, $J$=7 Hz), 1.1—1.8 (8H, m), 1.99 (1H, d, $J$=2 Hz, OH), 1.8—2.6 (6H, m), 3.79 (1H, dddd, $J$=7, 7, 4, 2 Hz), ca. 4.0 (2H, m), 4.11 (1H, ddd, $J$=8, 6, 4 Hz), 5.34 (1H, dt, $J$=15, 6 Hz), and 5.62 (1H, dt, $J$=15, 6 Hz); EI-MS (70 eV), $m/z$ 276, 274 (1:3; $M^+$), 239 (21; $M^+-Cl$), 221 (11), 207, 205 (3:9; $M^+-C_5H_9$), 177, 175 (4:14; $M^+-C_6H_{11}O$), 153 (17), 139 (20; $M^+-C_6H_{11}O-HCl$), 121 (38), 99 (8: $M^+-C_9H_{16}ClO$), 95 (74), 83 (31), 81 (41), 70 (21), 69 ($M^+-C_6H_{11}O-Cl-C_5H_{11}$), 67 (28), 57 (20), 55 (95), 43 (32), and 41 (100).

**Chlorination of 13 into 14.** A solution of **13**[17,20] (73 mg) in dry carbon tetrachloride (1 ml) was refluxed with triphenylphosphine (81 mg) for 23 h in $N_2$ atmosphere and then cooled. The subsequent removal of the solvent gave an oily substance which was chromatographed over silica gel with hexane–benzene (1:1) to afford **14** (46 mg); oil; $[\alpha]_D$ +23.2° ($c$ 0.860); IR (neat), $\nu_{max}$ 3030, 1740, 1240, 1095, 1065, 1035, 970, 945, and 710 cm$^{-1}$; $^1$H NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=7 Hz), 0.95 (3H, t, $J$=7 Hz), 1.1—1.7 (8H, m), 1.7—2.7 (6H, m), 2.07 (3H, s), 3.95 (2H, m, $W_H$=13 Hz), 4.24 (1H, ddd, $J$=8, 8, 5 Hz), 4.86 (1H, ddd, $J$=7, 6, 5 Hz), 5.32 (1H, dt, $J$=16, 7 Hz), and 5.57 (1H, dt, $J$=16, 6 Hz); EI-MS (70 eV), $m/z$ 318, 316 (0.1:0.3; $M^+$), 281 (0.7; $M^+-Cl$), 258, 256 (1:3; $M^+-CH_3COOH$), 229 (3), 221 (50; $M^+-Cl-CH_3COOH$), 177, 175 (1:3; $M^+-C_8H_{13}O_2$), 153 (66), 139 (4; $M^+-HCl-C_8H_{13}O_2$), 121 (14), 95 (19), 83 (7), 82 (9), 81 (17), 69 (15; $M^+-C_8H_{13}O_2-Cl-C_5H_{11}$), 67 (8), 55 (17), 43 (100), and 41 (19).

**Saponification of 14 into 15.** A solution of **14** (18 mg) and $K_2CO_3$ (50 mg) in MeOH (0.5 ml) was stirred for 1.5 h at room temperature under $N_2$ atmosphere, then water was added, and most of MeOH was evaporated in vacuo. The mixture was then extracted with ether and the ethereal solution was washed with saturated brine and dried over $Na_2SO_4$. After removal of the solvent, the residual oil was chromatographed over silica gel with hexane–benzene (1:3) to yield **15** (15 mg); oil; $[\alpha]_D$ +28.9° ($c$ 0.830); IR (neat), $\nu_{max}$ 3550, 3430, 3030, 1280, 1120, 1090, 1060, 1040, 970, and 720 cm$^{-1}$; $^1$H NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=6 Hz), 0.98 (3H, t, $J$=7Hz), 1.1—1.8 (8H, m), 2.10 (1H, d, $J$=6 Hz, OH), 1.8—2.5 (6H, m), 3.47 (1H, dddd, $J$=6, 6, 6, 6 Hz), 3.98 (2H, m), 4.09 (1H, ddd, $J$=9, 7, 5 Hz), 5.40 (1H, dt, $J$=16, 6 Hz), and 5.45 (1H, dt, $J$=16, 6 Hz); EI-MS (70 eV), $m/z$ 276, 274 (1:3; $M^+$), 239 (5; $M^+-Cl$), 221 (4; $M^+-H_2O-Cl$), 207, 205 (12:37; $M^+-C_5H_9$), 177, 175 (2:6; $M^+-C_6H_{11}O$), 169 (4; $M^+-C_5H_9-HCl$), 139 (8; $M^+-HCl-C_6H_{11}O$), 121 (28), 95 (68), 93 (14), 82 (24), 80 (46), 70 (31), 69 (67; $M^+-C_6H_{11}O-Cl-C_5H_{11}$), 67 (26), 57 (16), 55 (100), 42 (26), and 41 (68).

**Collins Oxidation of 11 into the Chloro Ketone 16.** Collins oxidation of **11** (12 mg) was carried out with dry chromium trioxide (30 mg) in dry pyridine (46 $\mu$l) and dry $CH_2Cl_2$ (1 ml) by the usual method to give an oily substance which was chromatographed over silica gel with hexane–benzene (1:3) to give **16** (9 mg); oil; $[\alpha]_D$ +85.0° ($c$ 0.367); IR (neat), $\nu_{max}$ 3030, 1715, 1305, 1300, 1115, 1075, 1045, and 970 cm$^{-1}$; $^1$H NMR (100 MHz) $\delta$=0.90 (3H, br t, $J$=6 Hz), 0.99 (3H, t, $J$=7 Hz), 1.1—1.8 (8H, m), 2.1 (2H, m), 2.40 (2H, m), 3.30 (2H, br d, $J$=5 Hz), 3.8—4.2 (2H, m), 4.58 (1H, t, $J$=8 Hz), and 5.3—5.8 (2H, m); EI-MS (70 eV), $m/z$ 274, 272 (0.7:2; $M^+$), 237 (1; $M^+-Cl$), 210 (7), 177, 175 (20:91; $M^+-C_6H_9O$), 139 (36; $M^+-C_6H_9O-HCl$), 121 (90), 95 (100), 93 (26), 80 (13), 78 (18), 69 (70; $M^+-C_6H_9O-Cl-C_5H_{11}$), 67 (20), 55 (74), 43 (22), and 41 (74).

**Collins Oxidation of 15 into the Chloro Ketone 16.** Collins oxidation of **15** (15 mg) was carried out in the same conditions as that in the case of the oxidation of **11** to afford, after the purification by means of silica-gel chromatography, a ketone (12 mg) which was identical with the chloro ketone **16** in all respects (IR, $^1$H NMR, MS, and specific rotation).

**Bromination of 11 into 17.** A solution of **11** (20 mg) in dry benzene (2 ml) was refluxed with triphenylphosphine (40 mg) and carbon tetrabromide (50 mg) for 30 min in $N_2$ atmosphere. The subsequent removal of the solvent gave a residual substance which was subjected to column chromatography over silica gel with hexane to yield **17** (11 mg); mp 122—123 °C (diisopropyl ether); $[\alpha]_D$ +27.6° ($c$ 0.808); IR ($CHCl_3$), $\nu_{max}$ 3030, 1665, 1120, 1095, 1070, 1040, 1020, 970, and 925 cm$^{-1}$; $^1$H NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=6 Hz), 0.98 (3H, t, $J$=7 Hz), 1.1—1.8 (8H, m), 2.0—2.8 (6H, m), 3.8—4.1 (3H, m), 4.27 (1H, ddd, $J$=7, 7, 4 Hz), 5.42 (1H, dt, $J$=15, 6 Hz),

and 5.63 (1H, dt, $J$=15, 5 Hz); EI-MS (70 eV), $m/z$ 340, 338, 336 (1:3:3; $M^+$), 303, 301 (12:12; $M^+-Cl$), 270, 268, 266 (1:3:3; $M^+-C_5H_9-H$), 259, 257 (3:9; $M^+-Br$), 221 (9: $M^+-Cl-Br-H$), 177, 175 (3:10; $M^+-C_6H_{10}Br$), 139 (7; $M^+-C_6H_{10}Br-HCl$), 121 (23), 111 (18), 107 (22), 95 (74), 83 (39), 81 (21), 79 (22), 69 (78; $M^+-C_6H_{10}Br-Cl-C_5H_{11}$), 67 (39), 55 (100), and 41 (97).

**Bromination of 15 into 18.** A solution of **15** (16 mg) in dry benzene (3 ml) was refluxed with triphenylphosphine (32 mg) and carbon tetrabromide (40 mg) for 30 min in $N_2$ atmosphere. After removal of the solvent, a residual oil was subjected to a column chromatography over silica gel with hexane to afford **18** (18 mg); oil; $[\alpha]_D$ +26.9° ($c$ 1.77); IR (neat), $\nu_{max}$ 3030, 1660, 1120, 1080, 1065, 1030, 970, 920, 720, and 705 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=6 Hz), 0.99 (3H, t, $J$=7 Hz), 1.1—2.8 (14H, m), 3.7—4.1 (3H, m), 4.22 (1H, ddd, $J$=7, 7, 7 Hz), 5.41 (1H, dt, $J$=15, 6 Hz), and 5.62 (1H, dt, $J$=15, 5 Hz); EI-MS (70 eV), $m/z$ 340, 338, 336 (1:3:3; $M^+$), 303, 301 (15:15; $M^+-Cl$), 259, 257 (3:9; $M^+-Br$), 258, 256 (1:3; $M^+-HBr$), 221 (11; $M^+-Cl-Br-H$), 177, 175 (3:10; $M^+-C_6H_{10}Br$), 151 (25), 139 (7; $M^+-C_6H_{10}Br-HCl$), 121 (22), 107 (23), 95 (59), 83 (26), 81 (23), 79 (22), 69 (55; $M^+-C_6H_{10}Br-Cl-C_5H_{11}$), 55 (100), and 41 (94).

**Conversion of 17 into 19.** To a solution of **17** (10 mg) in EtOH (1 ml) was added W-7 Raney nickel freshly prepared from Al-Ni alloy (2 g), and the mixture was stirred for 17 h at room temperature. After removal of the Ni, the solvent was evaporated to leave a residual oil which was chromatographed on column chromatography over silica gel with hexane–benzene (4:1) to give a chrolo ether **19** (5 mg); oil; $[\alpha]_D$ +21.6° ($c$ 0.190); IR (neat), $\nu_{max}$ 1280, 1245, 1120, 1090, 1070, 925, and 720 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, $J$=6 Hz), 0.89 (3H, br t, $J$=6 Hz), 1.1—1.8 (18H, m), 1.7—2.3 (2H, m), and 3.7—4.2 (3H, m); EI-MS (70 eV), $m/z$ 262, 260 (0.1:0.3; $M^+$), 191, 189 (3:9; $M^+-C_5H_{11}$), 177, 175 (30:100; $M^+-C_6H_{13}$), 139 (14; $M^+-C_6H_{13}-HCl$), 135 (23), 121 (24), 95 (36), 83 (30), 69 (54; $M^+-C_5H_{11}-C_6H_{13}-Cl$), 55 (75), 43 (42), and 41 (38).

**Conversion of 18 into 19.** To a solution of **18** (21 mg) in EtOH (1 ml) was added W-7 Raney nickel freshly prepared from Al-Ni alloy (2 g), and the mixture was stirred for 17 h at room temperature. After worked up as usual, the resulting oil was purified by silica-gel column chromatography with hexane–benzene (4:1) to yield an ether (10 mg) which was identical with the chloro ether **19** in all respects.

**Rearranged Product 22:** Oil; $[\alpha]_D$ +49.6° ($c$ 1.02); IR (neat), $\nu_{max}$ 1290, 1205, 1200, 1115, 1095, 1065, 1030, 1000, 970, 920, 780, and 740 $cm^{-1}$; $^1H$ NMR (400 MHz) $\delta$=0.89 (3H, br t, $J$=6.8 Hz), 1.00 (3H, t, $J$=7.3 Hz), 1.2—1.7 (9H, m), 1.75 (1H, dqd, $J$=15.1, 7.3, 3.9 Hz), 2.18 (1H, ddd, $J$=13.2, 8.3, 8.3 Hz), 2.33 (2H, dd, $J$=6.8, 6.8 Hz), 2.65 (1H, ddd, $\delta$=13.2, 6.8, 6.8 Hz), 3.86 (1H, ddd, $J$=8.3, 7.3, 6.8 Hz), 3.8—4.0 (3H, m), 4.06 (1H, ddd, $J$=7.3, 4.9, 4.9 Hz), and 4.21 (1H, ddd, $J$=6.8, 6.8, 5.7 Hz); EI-MS (70 eV), $m/z$ 371, 369, 367 (0.3:0.6:0.3; $M^+-C_2H_5$), 329, 327, 325 (0.7:1.4:0.7; $M^+-C_5H_{11}$), 319, 317 (1:1; $M^+-Br$), 318, 316 (1:1; $M^+-HBr$), 247, 245 (1:1; $M^+-C_5H_{11}-HBr$), 221, 219 (10:10; $M^+-C_6H_{10}BrO$), 179, 177 (14:14; $M^+-C_9H_{16}BrO$), 139 (95; $M^+-C_6H_{10}BrO-HBr$), 121 (25), 97 (100; $M^+-C_9H_{16}BrO-HBr$), 95 (26), 69 (60; $M^+-C_9H_{16}BrO-Br-C_5H_{11}$), 55 (20), and 41 (31). Found: $m/z$ 370.9845. Calcd for $C_{13}H_{21}{}^{81}Br_2O_2$: $M-C_2H_5$, 370.9867.

**Conversion of 10 into 23.** To a solution of **10** (18 mg) in EtOH (3 ml) was added W-7 Raney nickel freshly prepared from Al-Ni alloy (2 g), and the mixture was refluxed for 3.5 h. After worked up as usual, the resulting oil was purified by silica-gel column chromatography with hexane–benzene (1:3) to yield a dehalogenated ether **23** (10 mg); oil; $[\alpha]_D$ −14.5° ($c$ 0.518); IR (neat), $\nu_{max}$ 1090, 1070, 1040, and 930 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, $J$=7 Hz), 0.90 (3H, t, $J$=7 Hz), 1.1—2.0 (16H, m), 1.9—2.1 (2H, m), and 3.7—4.0 (4H, m); EI-MS (70 eV), $m/z$ 240 (0.2; $M^+$), 211 (1; $M^+-C_2H_5$), 169 (1; $M^+-C_5H_{11}$), 141 (43; $M^+-C_6H_{11}O$), 140 (11; $M^+-C_2H_5-C_5H_{11}$), 123 (46), 99 (79; $M^+-C_9H_{17}O$), 98 (23), 81 (100), 67 (14), and 55 (37).

**Conversion of 22 into 23.** To a solution of **22** (18 mg) in EtOH (2 ml) was added W-7 Raney nickel freshly prepared from Al-Ni alloy (2 g), and the mixture was stirred for 1.5 h at room temperature. After worked up as usual, the residual oil was purified by silica-gel column chromatography with hexane–benzene (1:3) to give a debrominated ether (11 mg) which was identical with the ether **23** in all respects.

**Partial Degradation of 22.** To a solution of **22** (257 mg) and AcOH (400 $\mu$l) in MeOH (5 ml) was gradually added activated zinc dust (800 mg) with stirring for 2.5 h at room temperature under $N_2$ atmosphere. After the usual work-up, the resulting oil was subjected to column chromatography over silica gel with hexane–benzene (2:1) to afford three products, **24** (52 mg), **25** (101 mg), and **26** (24 mg).

**24:** Oil; $[\alpha]_D$ +28.5° ($c$ 1.12); IR (neat), $\nu_{max}$ 3560, 3430, 3030, 1280, 1120, 1080, 1065, 1045, 1025, 970, and 925 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=6 Hz), 0.98 (3H, t, $J$=7 Hz), 1.1—1.8 (8H, m), 2.01 (1H, d, $J$=3 Hz; OH), 2.0—2.3 (5H, m), 2.50 (1H, ddd, $J$=14, 8, 8 Hz), 3.80 (1H, dddd, $J$=7, 7, 4, 3 Hz), 3.8—4.2 (3H, m), 5.38 (1H, dt, $J$=15, 6 Hz), and 5.62 (1H, dt, $J$=15, 5 Hz); EI-MS (70 eV), $m/z$ 320, 318 (1:1; $M^+$), 302, 300 (0.5:0.5; $M^+-H_2O$), 251, 249 (2:2; $M^+-C_5H_9$), 250, 248 (2:2; $M^+-C_5H_9-H$), 239 (12; $M^+-Br$), 221 (12; $M^+-H_2O-Br$), 221, 219 (3:3; $M^+-C_6H_{11}O$), 169 (5; $M^+-C_5H_9-HBr$), 151 (25), 139 (37; $M^+-C_6H_{11}O-HBr$), 121 (32), 99 (9; $M^+-C_9H_{16}BrO$), 95 (52), 83 (21), 81 (44; $M^+-C_9H_{16}BrO-H_2O$), 69 (66; $M^+-C_6H_{11}O-Br-C_5H_{11}$), 67 (23), 57 (14), 55 (100), 43 (23), and 41 (70).

**25:** Mp 36—37 °C (hexane); $[\alpha]_D$ +6.50° ($c$ 1.00); IR (Nujol), $\nu_{max}$ 3560, 3440, 3030, 1320, 1300, 1290, 1110, 1080, 1070, 1020, 980, 970, 935, and 920 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, $J$=7 Hz), 1.00 (3H, t, $J$=7 Hz), 1.1—1.9 (8H, m), 2.04 (1H, d, $J$=2 Hz; OH), 1.9—2.7 (6H, m), 3.7—4.1 (4H, m), 5.36 (1H, dt, $J$=15, 6 Hz), and 5.57 (1H, dt, $J$=15, 6 Hz); EI-MS (70 eV), $m/z$ 320, 318 (1:1; $M^+$), 302, 300 (1:1; $M^+-H_2O$), 263, 261 (0.3:0.3; $M^+-C_4H_9$), 245, 243 (0.3:0.3; $M^+-H_2O-C_4H_9$), 239 (3; $M^+-Br$), 221 (8; $M^+-Br-H_2O$), 209, 207 (3:3; $M^+-C_8H_{15}$), 181 (2; $M^+-HBr-C_4H_9$), 179, 177 (4:4; $M^+-C_9H_{17}O$), 149, 147 (2:2; $M^+-C_9H_{17}O-C_2H_5-H$), 141 (2; $M^+-C_6H_{10}BrO$), 97 (65; $M^+-C_9H_{17}O-HBr$), 81 (17), 69 (100; $M^+-C_9H_{17}O-Br-C_2H_5$), 55 (16), and 41 (27).

**26:** Mp 95—96 °C (diisopropyl ether); $[\alpha]_D$ −3.90° ($c$ 1.04); IR (Nujol), $\nu_{max}$ 3300, 3200, 3030, 1045, 970, and 965 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.89 (3H, br t, $J$=7 Hz), 0.99 (3H, t, $J$=7 Hz), 1.1—1.6 (6H, m), 2.2 (2H, br d, $J$=3 Hz; OH×2), 1.7—2.4 (8H, m), 3.63 (2H, m), 5.40 (2H, dt, $J$=15, 6 Hz), 5.61 (1H, dt, $J$=15, 6 Hz), and 5.65 (1H, dt, $J$=15, 5 Hz); EI-MS (70 eV), $m/z$ 240 (1; $M^+$), 222 (2; $M^+-H_2O$), 204 (1; $M^+-H_2O\times2$), 171 (4; $M^+-C_5H_9$), 165 (1; $M^+-C_4H_9-H_2O$), 153 (8; $M^+-C_5H_9-H_2O$), 129 (5; $M^+-C_8H_{15}$), 111 (16; $M^+-C_7H_{13}O_2$), 93 (12), 81 (23), 79 (29), 70 (19; $M^+-C_6H_{11}O-C_5H_{11}$), 69 (96; $M^+-C_{10}H_{19}O_2$), 67 (19), 57 (19), 55 (100), 43 (19), and 41 (39).

**Bromination of 13 into 27.** A solution of **13** (88 mg) in dry

benzene (5 ml) was refluxed with triphenylphosphine (155 mg) and carbon tetrabromide (196 mg) for 1 h in $N_2$ atmosphere. After removal of the solvent, the residual oily substance was subjected to column chromatography on silica gel with hexane–benzene (1 : 1) to afford **27** (106 mg); oil; $[\alpha]_D$ +26.1° (*c* 1.21); IR (neat), $\nu_{max}$ 3030, 1740, 1235, 1120, 1090, 1035, 970, and 945 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.89 (3H, br t, *J*=6 Hz), 0.95 (3H, t, *J*=7 Hz), 1.1—2.5 (14H, m), 2.06 (3H, s), 3.96 (2H, m), 4.24 (1H, ddd, *J*=8, 8, 5 Hz), 4.87 (1H, ddd, *J*=7, 6, 5 Hz), 5.32 (1H, dt, *J*=15, 6 Hz), and 5.58 (1H, dt, *J*=15, 5 Hz); EI-MS (70 eV), *m/z* 362, 360 (0.2 : 0.2; $M^+$), 302, 300 (2 : 2; $M^+-CH_3COOH$), 221 (64; $M^+-CH_3COOH-Br$), 153 (29), 139 (14; $M^+-C_8H_{13}O_2-HBr$), 121 (13), 111 (22), 95 (16), 81 (13), 80 (13), 69 (28; $M^+-C_8H_{13}O_2-Br-C_5H_{11}$), 55 (22), 43 (100), and 41 (17).

**Saponification of 27 into 28.** A solution of **27** (31 mg) and $K_2CO_3$ (100 mg) in MeOH (1 ml) was stirred for 1.5 h at room temperature under $N_2$ atmosphere. After the usual work-up, the resulting oily substance was chromatographed on silica-gel column with hexane–benzene (1 : 3) to yield **28** (25 mg); oil; $[\alpha]_D$ +32.4° (*c* 1.14); IR (neat), $\nu_{max}$ 3540, 3430, 3030, 1120, 1090, 1055, 1035, and 970 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.90 (3H, br t, *J*=6 Hz), 0.98 (3H, t, *J*=7 Hz), 1.1—2.6 (14H, m), 2.12 (1H, d, *J*=6 Hz; OH), 3.48 (1H, dddd, *J*=6, 6, 6, 6 Hz), 3.7—4.2 (3H, m), 5.42 (1H, dt, *J*=15, 6 Hz), and 5.62 (1H, dt, *J*=15, 5 Hz); EI-MS (70 eV), *m/z* 320, 318 (1 : 1; $M^+$), 251, 249 (26 : 26; $M^+-C_5H_9$), 239 (13; $M^+-Br$), 221 (15; $M^+-H_2O-Br$), 169 (27; $M^+-C_5H_9-HBr$), 151 (16), 139 (31; $M^+-C_6H_{11}O-HBr$), 133 (10), 123 (13), 121 (31), 95 (71), 83 (27), 81 (58; $M^+-C_9H_{16}BrO$), 70 (34), 69 (87; $M^+-C_6H_{11}O-Br-C_5H_{11}$), 67 (32), 57 (27), 55 (100), 43 (37), and 41 (85).

**Collins Oxidation of 24 into the Bromo Ketone 29.** Collins oxidation of **24** (12 mg) was carried out with dry chromium trioxide (31 mg) and dry pyridine (50 $\mu$l) in dry $CH_2Cl_2$ (1.2 ml) under the same conditions as that in the case of the oxidation of **11** to give an oily substance which was purified by silica-gel column chromatography with hexane–benzene (3 : 1) to yield **29** (10 mg); oil; $[\alpha]_D$ +66.3° (*c* 0.563); IR (neat), $\nu_{max}$ 3030, 1720, 1300, 1115, 1070, and 970 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.90 (3H, br t, *J*=6 Hz), 0.99 (3H, t, *J*=7 Hz), 1.2—1.7 (8H, m), 2.2 (2H, m), 2.49 (2H, m), 3.30 (2H, br d, *J*=5 Hz), 3.92 (1H, ddd, *J*=6, 5, 5 Hz), 4.15 (1H, m), 4.58 (1H, dd, *J*=8, 8 Hz), and 5.3—5.8 (2H, m); EI-MS (70 eV), *m/z* 318, 316 (2 : 2; $M^+$), 221, 219 (16 : 16; $M^+-C_6H_9O$), 203, 201 (5 : 5), 139 (68; $M^+-C_6H_9O-HBr$), 121 (94), 95 (97), 69 (91; $M^+-C_6H_9O-Br-C_5H_{11}$), 67 (16), 55 (70), 43 (19), and 41 (100).

**Collins Oxidation of 28 into the Bromo Ketone 29.** Collins oxidation of **28** (12 mg) was carried out under the same conditions as that in the case of the oxidation of **24** to afford a ketone (10 mg) which was identical with the bromo ketone **29** in all respects.

**Bromination of 25 into 30.** Bromination of **25** (130 mg) was performed with triphenylphosphine (210 mg) and carbon tetrabromide (270 mg) in dry benzene (20 ml) to give an oily substance, which was chromatographed over silica gel with hexane to yield a dibromide **30** (80 mg); oil; $[\alpha]_D$ +26.5° (*c* 1.23); IR (neat), $\nu_{max}$ 3020, 1295, 1110, 1070, 1060, 1010, 970, and 930 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, *J*=6 Hz), 1.00 (3H, t, *J*=7 Hz), 1.1—2.8 (14H, m), 3.86 (1H, ddd, *J*=8, 8, 7 Hz), 3.8—4.3 (3H, m), 5.41 (1H, dt, *J*=15, 6 Hz), and 5.60 (1H, dt, *J*=15, 6 Hz); EI-MS (70 eV), *m/z* 384, 382, 380 (0.2 : 0.4 : 0.2; $M^+$), 327, 325, 323 (0.3 : 0.6 : 0.3; $M^+-C_4H_9$), 303, 301 (5 : 5; $M^+$-Br), 221 (5; $M^+-HBr-Br$), 205, 203 (1 : 1; $M^+-C_6H_{10}BrO$), 179, 177 (5 : 5; $M^+-C_9H_{16}Br$), 97 (79; $M^+-C_9H_{16}Br-HBr$), 81 (11), 79 (11), 69 (100; $M^+-C_9H_{16}Br-Br-C_2H_5$), 67 (23), 57 (20), 55 (31), 43 (10), and 41 (64).

**Partial Degradation of 30.** To a solution of **30** (82 mg) and AcOH (400 $\mu$l) in MeOH (5 ml) was gradually added activated zinc dust (1.5 g) with stirring for 2 h at room temperature under $N_2$ atmosphere. After the usual work-up, the resulting oil was chromatographed on silica gel with hexane–benzene (3 : 1) to afford three products **31** (22 mg), **32** (21 mg), and **33** (12 mg).

**31:** Oil; $[\alpha]_D$ −18.0° (*c* 1.68); IR (neat), $\nu_{max}$ 3530, 3380, 3020, 1100, 1055, and 970 $cm^{-1}$. $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, *J*=7 Hz), 1.01 (3H, t, *J*=7 Hz), 1.1—2.2 (10H, m), 1.94 (1H, d, *J*=3 Hz; OH), 2.4—2.9 (4H, m), 3.64 (1H, m), 4.14 (1H, ddd, *J*=7, 7, 4 Hz), and 5.1—5.8 (4H, m); EI-MS (70 eV), *m/z* 304, 302 (0.1 : 0.1; $M^+$), 286, 284 (0.1 : 0.1; $M^+-H_2O$), 275, 273 (0.1 : 0.1; $M^+-C_2H_5$), 223 (3; $M^+-Br$), 205 (4; $M^+-H_2O-Br$), 165 (1; $M^+-C_4H_9-HBr$), 153, 151 (1 : 1; $M^+-C_{11}H_{19}$), 95 (15), 93 (14), 85 (15), 81 (20), 79 (29), 69 (40), 67 (38), 59 (16; $M^+-C_{12}H_{20}Br$), 57 (100; $M^+-C_{11}H_{18}BrO$), 55 (42), 43 (26), and 41 (58).

**32:** Oil; $[\alpha]_D$ −10.8° (*c* 1.68); IR (neat), $\nu_{max}$ 3530, 3400, 3020, 1665, 1080, 1060, 1035, and 970 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, *J*=7 Hz), 0.98 (3H, t, *J*=7 Hz), 1.1—1.5 (6H, m), 1.91 (1H, d, *J*=8 Hz; OH), 1.7—2.2 (4H, m), 2.31 (2H, dd, *J*=6, 6 Hz), 2.66 (2H, dd, *J*=6, 6 Hz), 3.53 (1H, dtd, *J*=8, 7, 3 Hz), 4.06 (1H, ddd, *J*=8, 7, 3 Hz), 5.36 (1H, dt, *J*=15, 7 Hz), 5.39 (1H, dt, *J*=15, 5 Hz), 5.52 (1H, dt, *J*=15, 6 Hz), and 5.65 (1H, dt, *J*=15, 6 Hz); EI-MS (70 eV) *m/z* 304, 302 (0.4 : 0.4; $M^+$), 286, 284 (0.2 : 0.2; $M^+-H_2O$), 235, 233 (2 : 2; $M^+-C_5H_9$), 223 (2; $M^+-Br$), 222 (1; $M^+-HBr$), 206 (2; $M^+-Br-OH$), 205 (8; $M^+-Br-H_2O$), 153 (13; $M^+-C_5H_9-HBr$), 135 (14), 83 (12), 81 (14), 70 (61; $M^+-C_9H_{16}Br-C_2H_5$), 69 (100; $M^+-C_{10}H_{18}BrO$), 67 (26), 57 (14), 55 (85), and 41 (81).

**33:** Oil; IR (neat), $\nu_{max}$ 3020, 1075, and 970 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, t, *J*=7 Hz), 0.97 (3H, br t, *J*=7 Hz), 1.1—1.5 (6H, m), 1.7—2.2 (4H, m), 2.5—2.9 (4H, m), and 5.44 (6H, m); EI-MS (70 eV), *m/z* 206 (1; $M^+$), 177 (1; $M^+-C_2H_5$), 150 (2), 149 (1; $M^+-C_4H_9$), 121 (3), 108 (14), 95 (64), 93 (29), 81 (33), 80 (32), 79 (82), 69 (17), 67 (100), 57 (13), 55 (42), 43 (32), and 41 (86).

**Hydrogenation of 31.** Hydrogenation of **31** (14 mg) was performed in EtOH over $PtO_2$-catalyst. After removal of the catalyst and the solvent, the residual oil was chromatographed over silica gel with hexane–benzene (3 : 1) to give a saturated bromohydrin **34** (11 mg); oil; $[\alpha]_D$ −26.7° (*c* 0.890); IR (neat), $\nu_{max}$ 3530, 3400, 1295, 1220, 1105, 1095, 1050, and 970 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.88 (3H, br t, *J*=6 Hz), 1.02 (3H, t, *J*=7 Hz), 1.1—2.0 (22H, m), 1.97 (1H, d, *J*=6 Hz; OH), 3.61 (1H, dddd, *J*=7, 6, 5, 3 Hz), and 4.18 (1H, ddd, *J*=9, 5, 3 Hz); EI-MS (70 eV), *m/z* 279, 277 (0.2 : 0.2; $M^+-C_2H_5$), 227 (0.2; $M^+-Br$), 226 (0.1; $M^+-Br$), 197 (1; $M^+-C_2H_5-HBr$), 149 (2), 71 (6), 59 (100; $M^+-C_{12}H_{24}Br$), 58 (5), 57 (24), 55 (5), 43 (21), and 41 (7).

**Bromination of Octahydrodeacetyllaurencin (35)[6] into 36.** Bromination of **35** (400 mg) was performed with triphenylphosphine (655 mg) and carbon tetrabromide (830 mg) in dry benzene (15 ml) to give an oily substance which was chromatographed over silica gel with hexane to yield a dibromide **36** (406 mg); oil; $[\alpha]_D$ −2.50° (*c* 1.08); IR (neat), $\nu_{max}$ 1185, 1115, 1090, 1070, and 1050 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.90 (3H, br t, *J*=6 Hz), 0.99 (3H, t, *J*=7 Hz), 1.1—2.2 (18H, m), 3.4—3.8 (2H, m), and 3.8—4.2 (2H, m); EI-MS (70 eV), *m/z* 386, 384, 382 (0.1 : 0.2 : 0.1; $M^+$), 305, 303 (0.6 : 0.6; $M^+-Br$), 304,

302 (0.3 : 0.3; $M^+-HBr$), 247, 245 (9 : 9; $M^+-HBr-C_4H_9$), 221, 219 (4 : 4; $M^+-C_6H_{12}Br$), 165 (38), 139 (34; $M^+-C_6H_{12}Br-HBr$), 111 (12; $M^+-C_6H_{12}Br-Br-C_2H_5$), 109 (50), 97 (32), 95 (86), 81 (60), 79 (50), 69 (100), 67 (65), 55 (83), and 41 (66).

**Partial Degradation of 36.** To a solution of **36** (264 mg) and AcOH (800 $\mu$l) in MeOH (10 ml) was gradually added activated zinc dust (1.5 g) with stirring for 4 h at room temperature under $N_2$ atmosphere. After the usual work-up, the resulting oily substance was subjected to repeated silica-gel column chromatography with hexane–benzene (3 : 1) to yield **37** (40 mg) and **38** (125 mg).

**37:** Oil; $[\alpha]_D$ −28.9° (*c* 1.50); IR (neat), $\nu_{max}$ 3400, 3020, 1655, 1295, 1230, 1100, 1070, 1050, and 970 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.89 (3H, br t, *J*=6 Hz), 1.02 (3H, t, *J*=7 Hz), 1.1—2.2 (19H, m), 3.60 (1H, m), 4.17 (1H, ddd, *J*=8, 6, 4 Hz), and 5.37 (2H, m); EI-MS (70 eV), *m/z* 306, 304 (1 : 1; $M^+$), 288, 286 (2 : 2; $M^+-H_2O$), 277, 275 (0.3 : 0.3; $M^+-C_2H_5$), 249, 247 (0.3 : 0.3; $M^+-C_4H_9$), 225 (1; $M^+-Br$), 207 (19; $M^+-H_2O-Br$), 151 (5; $M^+-OH-Br-C_4H_9$), 123 (35), 111 (10; $M^+-C_7H_{14}BrO$), 109 (60), 97 (16), 95 (100), 83 (19), 81 (65), 69 (83), 67 (55), 59 (79; $M^+-C_{12}H_{22}Br$), 57 (19), 55 (82), and 41 (60).

**38:** Oil; $[\alpha]_D$ −23.8° (*c* 0.608); IR (neat), $\nu_{max}$ 3400, 3020, 1650, 1305, 1280, 1260, 1115, 1070, 1040, 1010, and 965 $cm^{-1}$; $^1H$ NMR (100 MHz) $\delta$=0.90 (3H, br t, *J*=6 Hz), 0.96 (3H, t, *J*=7 Hz), 1.1—2.2 (18H, m), 3.69 (1H, m), 4.18 (1H, ddd, *J*=8, 5, 3 Hz), and 5.4 (2H, m); EI-MS (70 eV), *m/z* 306, 304 (0.6 : 0.6; $M^+$), 288, 286 (0.3 : 0.3; $M^+-H_2O$), 225 (3; $M^+-Br$), 207 (6; $M^+-Br-H_2O$), 141 (7; $M^+-C_6H_{12}Br$), 123 (57), 109 (12), 95 (56), 82 (15), 81 (100), 69 (41; $M^+-C_{10}H_{20}BrO$), 67 (62), 57 (11), 55 (71), 43 (13), and 41 (61).

**Hydrogenation of 37.** Hydrogenation of **37** (18 mg) was performed in EtOH over $PtO_2$-catalyst. After removal of the catalyst and the solvent, the resulting oily substance was purified by silica-gel column chromatography with hexane–benzene (3 : 1) to give a saturated bromohydrin (18 mg) which was identical with the bromohydrin **34** in all respects.

**Treatment of 39 with Activated Silica Gel.** A mixture of **39** (31 mg) and silica gel (Merck, Kieselgel 60, 70—230 mesh) (1.5 g), which was activated at 140 °C for 3 h, in hexane was stirred at room temperature for 24 h. After the silica gel was filtered off and washed with ethyl acetate, the combined solvents were evaporated to leave an oily substance which was chromatographed on silica-gel column with hexane–benzene (1 : 1) to yield hexahydronotoryne (**10**) (31 mg).

**Treatment of 39 with Silica Gel.** A solution of **39** (20 mg) and silica gel (Merck, Kieselgel 60, 70—230 mesh) (1 g) in hexane (10 ml) was stirred at room temperature for 24 h. After being worked up as described above, the residual oily substance was chromatographed on silica-gel column with hexane–benzene (1 : 1) to give hexahydronotoryne (**10**) (4 mg) and hexahydrolaurefucin (**21**) (16 mg).

**Treatment of 39 with Aluminum Oxide.** A solution of **39** (19 mg) and aluminum oxide (Merck, activity II-III) (1 g) in hexane (10 ml) was stirred at room temperature for 20 h. After the aluminum oxide was filtered off and then washed with ethyl acetate, the combined solvents were evaporated to give an oily substance which was chromatographed on silica-gel column with hexane–benzene (1 : 1) to yield hexahydronotoryne (**10**) (4 mg) and hexahydrolaurefucin (**21**) (15 mg).

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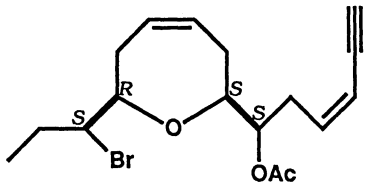


**74**

Fig. 3.

**74:** $C_{17}H_{23}BrO_3$, $[\alpha]_D$ −25.7° (*c* 0.737; $CHCl_3$), $^1H$ NMR (270 MHz, $CDCl_3$) $\delta$=1.06 (3H, t, *J*=7.3 Hz), 2.09 (3H, s), 3.12 (1H, d, *J*=2.2 Hz), 3.48—3.58 (2H, m), 3.90—3.97 (1H, m), 5.04 (1H, ddd, *J*=7.7, 4.9, 4.9 Hz), 5.56 (1H, br d, *J*=10.6 Hz), 5.78 (2H, m), and 6.00 (1H, ddd, *J*=10.6, 7.0, 7.0 Hz); $^{13}C$ NMR (67.9 MHz, $CDCl_3$) $\delta$=12.15 (q), 21.19 (q), 27.39(t), 31.69 (t), 32.67 (t), 34.50 (t), 61.52 (d), 74.51 (d), 77.23 (d), 80.05 (d), 82.26 (s), 82.88 (d), 110.88 (d), 128.85 (d), 128.89 (d), 140.38 (d), and 170.68 (s).

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