11. The Absolute Configurations and Biogenesis of Some New Halogenated Chamigrenes from the Sea Hare *Aplysia dactylomela*

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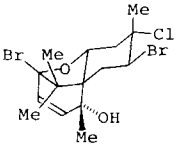
Four new halogenated chamigrenes have been isolated from the sea hare, the (*E*)- and (*Z*)-9-(bromomethylidene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-ones (**11** and **10**, resp.) the structures of which were deduced by NMR spectroscopy and by comparison with a known relative, the (8*R*,9*R*)-8-bromo-9-chloro-5,5,9-trimethyl-1-methylidenespiro[5,5]undec-3-en-2-one (**12**), and its (11*R*)-11-acetoxy-substituted derivative **13**. Their structures and absolute configurations were determined and deduced by X-ray using the absolute-structure parameter. The configurations were remarkable in being enantiomeric to those of the tertiary chlorochamigrenes isolated so far. Consequently, a more general scheme is proposed to account for their biogenesis.

Introduction. – The algal genus *Laurencia*, a red sea weed, is a rich source of halogenated sesquiterpenes [1]. Ever since the discovery of pacifenol (**1**), a tricyclic chamigrene structure, in 1971 [2], some 25 other chlorobromochamigrenes have been isolated from



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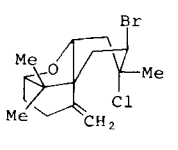

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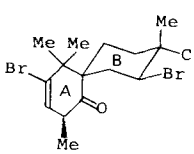

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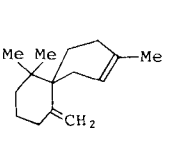

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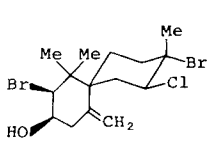

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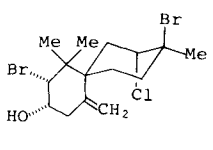

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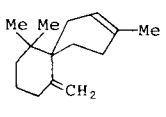

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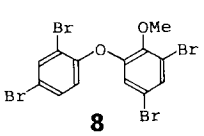

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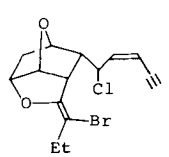

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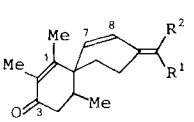
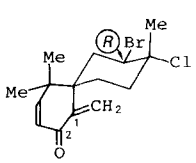


10 R^1= H, R^2= Br
11 R^1= Br, R^2= H



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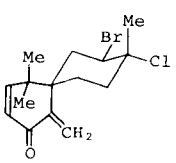
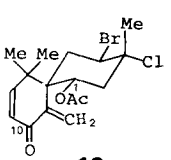


12′



13

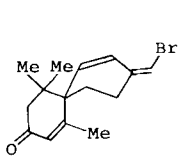
Laurencia and from sea hares which feed on it. About 20 of these metabolites contain secondary Br- and tertiary Cl-substituents in ring B. Representative examples are provided by nidifocene (**2**) [3], a relative of **1**, and kylinone (**3**) [4]. Apart from the characteristic halogenation pattern, members of this class all have absolute configurations related to that of (−)-β-chamigrene (**4**). The remaining five or so chamigrenes are different in that they contain secondary Cl- and tertiary Br-substituents. Some of these, exemplified by obtusol (**5**) [5], have absolute configurations based on that of **4**, while others, in particular isoobtusol (**6**) [6], are structurally related to (+)-β-chamigrene (**7**).

In the present paper we describe the isolation of two known, non-terpenoid compounds **8** and **9** and the four new halogenated chamigrenes **10**–**13** from *Aplysia dactylomela*. The absolute configurations of **12** and **13** have been determined and deduced by using the absolute-structure parameter [7]. Although **12** and **13** belong to the class of chamigrenes bearing secondary Br- and tertiary Cl-substituents, they are novel as they are enantiomeric to the other members. Consequently, their biogenesis is not accommodated by currently accepted schemes.

Results. – The digestive glands of six individuals of *A. dactylomela* were excised and homogenized with acetone. The resulting oil, on evaporation of acetone, was then extracted with hexane and AcOEt. The hexane extract, on chromatography, gave 2,4-dibromo-6-(2′,4′-dibromophenoxy)anisole (**8**), *cis*-maneonene C (**9**), and the three halogenated chamigrenes **10**, **12**, and **13**. Chromatographic separation of the AcOEt extract afforded **9**, **10**, and its isomer **11**.

The identity of diphenyl ether **8**, which was only isolated in a small amount, was ascertained by comparing its TLC and ^{1}H-NMR spectra with those of the same compound isolated [8] from the green alga *Cladophora fascicularis* collected at the same site as that of the sea hare. The C_{15}-enyne **9** was obtained as an unstable oil. However, its identity was established by comparison of its spectral (^{1}H- and ^{13}C-NMR, EI-MS) data with that reported for an authentic sample [9].

Chamigrene **10** was obtained as an unstable crystalline solid from both the hexane and AcOEt extracts. The molecular formula $C_{15}H_{19}BrO$ requires six sites of unsaturation. The IR (1645, 1605 cm^{-1}) and UV spectra (λ_{max} 253 nm) are indicative of an α,β-unsaturated ketone function. The ^{13}C-NMR spectrum displays signals characteristic of a carbo-



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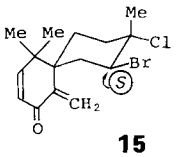

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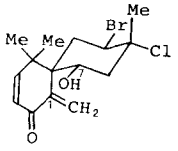

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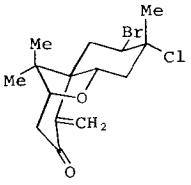

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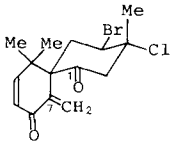

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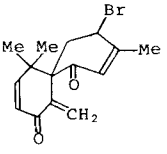

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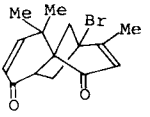

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nyl group (197.8 ppm) and three double bonds (159.9 (*s*), 138.6 (*d*), 136.4 (*s*), 131.4 (*s*), 127.4 (*d*), and 102.8 (*d*) ppm). These data suggest that **10** is a bicyclic sesquiterpene. In fact, comparison with the data reported by *Kurosawa* [10] for the chamigrene **14** reveals that the two structures are closely related. The virtually identical ^{1}H-NMR signals for the vinyl protons at C(7), C(8), and for BrC*H*= of the two compounds means that they have identical B rings. Only the A rings are different. Compound **10** has *two* vinyl CH_3 groups (1.85, 1.77 ppm) and *one* secondary CH_3 group (0.97 ppm), whereas **14** possesses a single vinyl CH_3 group (1.88 ppm), a geminal $(CH_3)_2$ grouping (1.03, 1.06 ppm), and a single vinyl proton (5.77 ppm) in ring A. Consequently, the structure can be correctly formulated as **10**. The presence of the α-CH_3 substituent in **10** accounts for the bathochromic shift of 13 nm in the UV spectrum when compared with that of **14**. Like **14**, **10** isomerized easily to **11**, thereby suggesting that the latter is simply an artefact of isolation.

After several attempts, the chamigrene **12** could finally be induced to crystallize from hexane/CCl_4. Its IR and ^{1}H-NMR spectra are identical with those of the chamigrene derivative **15** isolated from *L. nipponica* by *Suzuki* [11]. In contrast, the optical rotation $[\alpha]_D$ of our sample is +19.6°, while that of *Suzuki*'s was reported to be −10.7°. Evidently, the two samples are enantiomers. Confirmation of this relation was obtained by X-ray analysis using the absolute-structure parameter. The configuration of **12** is enantiomeric with that of **15** *(Fig. 1)*. It is seen that in the solid state the cyclohexenone ring adopts the

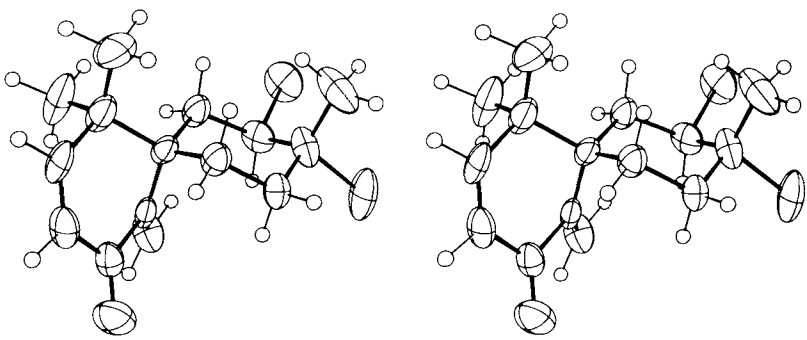


Fig. 1. *Stereoscopic view of the structure of bromochlorochamigrene* **12**

envelope conformation in which the methylidene group points towards the bromomethine group (see **12**). However, in solution at room temperature, the other conformation **12′** is also populated as attested by the ^{1}H-NMR spectrum which displays two sets of signals for the bromomethine proton. The signals at lower field can be attributed to conformation **12** where the bromomethine proton lies in the plane of the exocyclic double bond and is thus deshielded. A similar conformational effect has already been observed by *Suzuki* [11] for the enantiomer **15**.

Compound **13** was isolated as a crystalline solid in 29% yield from the hexane extract. The EI-MS fragment ion clusters are indicative of an AcO group. The ^{1}H-NMR, IR, and UV spectral features are those expected of the methylidene and dienone entities. Furthermore, the comparison of the ^{1}H- and ^{13}C-NMR spectra of **12** and **13** showed that they have the same hydrocarbon skeleton. As **13** has the molecular formula $C_{17}H_{22}BrClO_3$, it must be structurally the same as **12**, except that it possesses an AcO

group. In order to determine the position of the latter, **13** was treated with 1% KOH/EtOH. An alcohol **16** and an ether **17** were obtained in roughly 1:2 ratio. Treatment of **16** with *p*-toluenesulfonic acid and refluxing benzene also afforded the ether **17**. The ^{1}H-NMR spectrum of **17** still reveals the methylidene protons, but the signals due to the *cis*-olefinic protons as seen in **13** and **16** are absent. Instead, the spectrum shows a complex signal at 4.06 ppm characteristic of two methine groups attached to an O-atom, compatible with a cyclic-ether structure for **17**. The ready cyclization of **16** suggested that the AcO group in **13** is close to the α,β-unsaturated ketone function, possibly located next to the spiro atom. Once again, confirmation was secured by X-ray crystallographic analysis. The absolute configuration of **17** *(Fig. 2)* is the same as that of **12**.

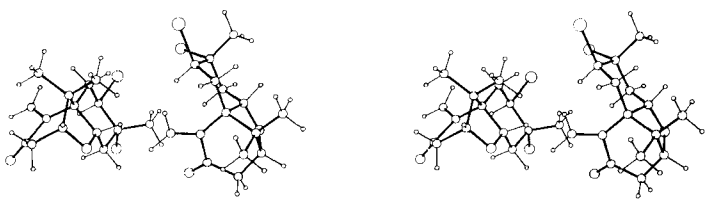


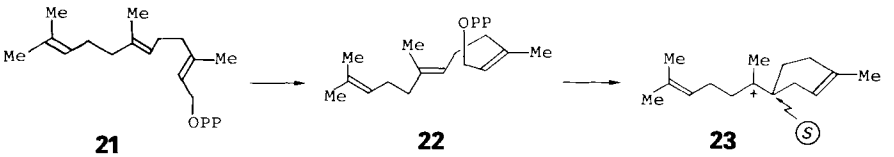
Fig. 2. *Stereoscopic view of the structures of two independent molecules of tricyclic bromochlorochamigrene* **17**

Oxidation of **16** with *Jones* reagent furnished the diketone **18**. When a solution of **18** in 0.1% KOH was allowed to stand at room temperature for 1 h, dehydrochlorination occurred to give the α,β-unsaturated γ-bromo ketone **19** in 73% yield. On the other hand, when a solution of **18** in 0.5% KOH/EtOH was kept at room temperature for 12 min, the tricyclic ketone **20** formed in 52% yield. Its structure was deduced in straightforward fashion. The presence of two enone moieties was revealed by the characteristic UV absorption (λ_{max} 233 nm) and the IR bands (1660 and 1620 cm^{-1}). The ^{1}H-NMR spectrum shows resonances due to two *cis*-disposed olefinic protons (6.71 and 5.92 ppm) and a vinyl proton (5.72 ppm) coupled allylically to a CH_3 group. No signals are seen for methylidene protons. Since the molecular formula of **20** is $C_{15}H_{17}BrO_2$ and as the two enone moieties account for four of the required seven degrees of unsaturation, it follows that **20** must be a tricyclic compound. It undoubtedly arises by intramolecular *Michael* addition of **19**. The intermediacy of **19** was confirmed by its conversion on base treatment to **20**.

Discussion. – All the metabolites isolated reflect the particular diet of the sea hare. The tetrabromo compound **8** is yet another example of the class of polybrominated diphenyl ethers similar to those found in the sponge *Dysidea herbacea* [12] and the acorn worm *Ptychodera flava laysanica* [13]. The provenance of *cis*-maneonene-C (**9**) undoubtedly arises from ingested algae which are the same as or related to the green variety of *L. nidifica* collected off Oahu, Hawaii [9].

The pair of isomeric spirocyclic trienones **10** and **11** now brings the number of such structures to ten [10] [14]. They all display lability about the exocyclic bromomethylidene grouping, probably through a protonation/deprotonation process. However, **10** and **11** are of interest in that they constitute the second example of a chamigrene having undergone rearrangement of a CH_3 group. As the first example [4] kylinone (**3**) was the result of a *Lewis* acid induced epoxide opening, it could be inferred that **10** springs from a

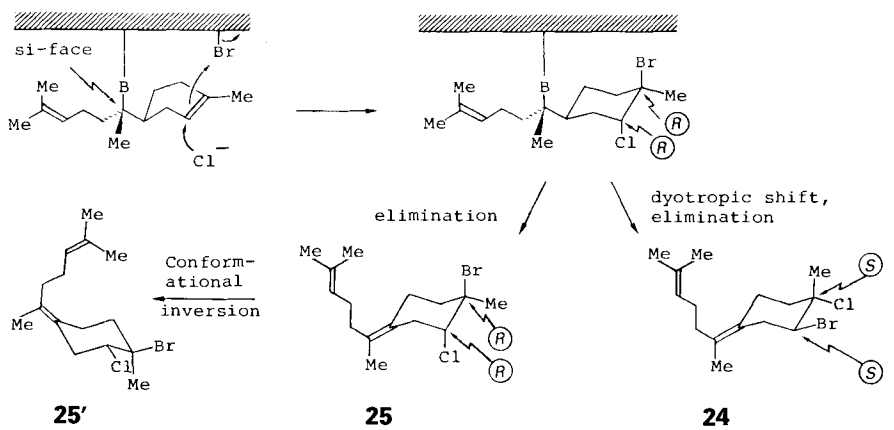
Scheme 1



mechanistically similar rearrangement. Of greater mechanistic significance are the two new halogenated chamigrenes **12** and **13**, because they constitute an exception to a biogenetic scheme which, although initially proposed [15] for sesquiterpenes produced by *Laurencia obtusa*, is regarded as having general validity.

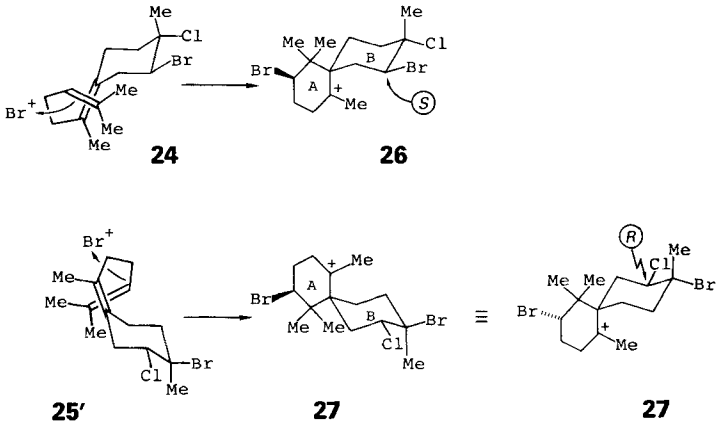
In order to appreciate the nature of the exception, the stereochemical aspects of the key steps proposed for *trans,trans*-farnesyl pyrophosphate (**21**) need to be analyzed *(Scheme 1)*. The very first step is the construction of ring B to yield the γ-bisabolyl cation (**23**) having the (*S*)-configuration at the newly created cyclohexenyl position, presumably by enzymic cyclization of the *cis,trans*-isomer **22** [16]. In order to undergo halogenation, this cation is then fixed on its *si*-face to the enzyme surface *(Scheme 2)*. Once attached,

Scheme 2



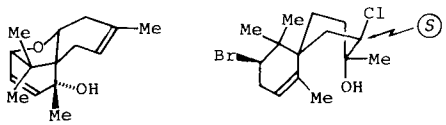
the cyclohexenyl moiety is correctly placed to receive a Br^+ ion from the enzyme surface on the *re*-face of the methylvinyl C-atom. At the same time, a free Cl-ion adds in diaxial manner to produce a cyclohexane ring bearing tertiary Br- and secondary Cl-substituents of the (*R,R*)-configuration. Subsequent detachment from the enzyme surface by *trans*-elimination uniquely gives the (*E*)-γ-bisabolene structure **25**. Next, the diaxial halogen substituents can either minimize non-bonding interactions by conformational inversion (**25**→**25'**) which leaves the configurations unchanged, or they can undergo dyotropic rearrangement [17] which produces the (*S,S*)-configuration at the two centers (see **24**). The resulting tertiary (*E*)-bromo- and tertiary (*E*)-chlorobisabolenes **25'** and **24**, respectively, are now ready to form ring A by a second cyclization *(Scheme 3)*. This time the juxtaposition of the three unsaturated centers *vis-a-vis* an enzyme-bound Br^+ ion is

Scheme 3



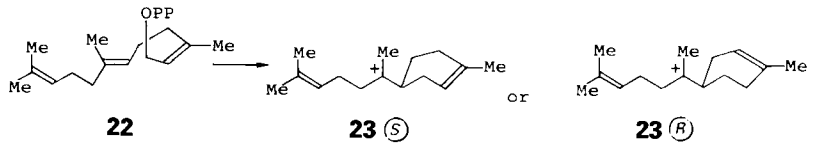
dictated by intramolecular steric considerations. The new C–C bond is created on the *si-si* and the *re-re* face of the tetrasubstituted double bonds of **24** and **25'**, respectively, thereby generating the spirocyclic cations **26** and **27** in each of which two secondary halogen substituents are disposed *cis*. Further evolution of these cations leads to the various metabolites.

This biogenetic scheme embodies all the stereochemical features displayed by most of the halogenated chamigrenes described so far. Even when halogenation failed to occur, the stereochemistry of the remaining stages still holds good. Some of the constituents of *L. nipponica* YAMADA provide a case in point; γ-bisabolene and its 8,9-epoxide possess the (*E*)-configuration [18], and the chamigrene **28** must have arisen from (*E*)-11-hydroxy-γ-bisabolene [19].

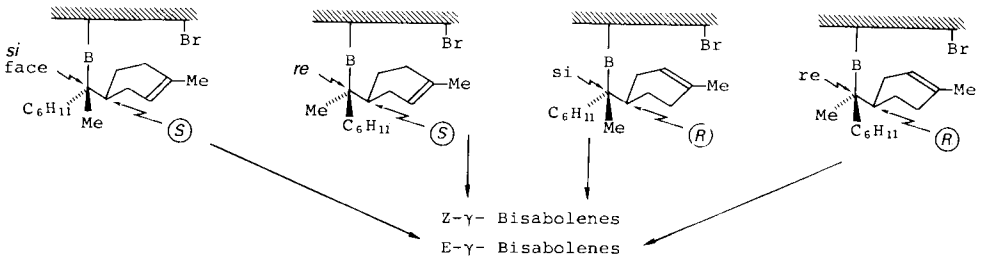


Despite its success, this scheme does not account for the formation of tertiary chlorochamigrenes where the secondary bromomethine groups in the B ring have the (*R*)-configuration, which is the case for the metabolites **12** and **13**. Clearly some of the stages, ring-B or bisabolyl-cation formation, fixation to the enzyme, halogenation, elimination with or without dyotropic shift, and ring-A formation are not immutable and variations should be possible. Inspection of the scheme reveals that only two stages are amenable to variation. The primary formation of ring B by cyclization of farnesyl pyrophosphate could occur in two ways to give a cyclohexenyl cation **23** having either the (*S*)- or the (*R*)-configuration *(Scheme 4)*. The resulting cations could then be fixed to the enzyme either on their *si*- or *re*-faces *(Scheme 5)*. In all the other stages the same canons of reactivity and stereochemistry will be respected as before.

Scheme 4



Scheme 5



Chlorobromination of ring B followed by elimination will give both (*E*)- and (*Z*)-γ-bisabolenes. Subsequent construction of ring A by bromination will create two different geometries of secondary substitution in the two rings (*Table 1*). (*E*)-Bisabolene will give rise to trihalochamigrenes in which the secondary Br-substituent (sec. Br) in ring A is *cis* to the secondary Cl- or Br-substituent (sec. X) in ring B; (*Z*)-bisabolenes will produce a *trans* relation.

Thus, the total number of reaction types will be four (1-N to 4-N) giving, in principle, four different tertiary bromochamigrenes and four different tertiary chlorochamigrenes when a dyotropic shift occurs (1-D to 4-D, *Table 1*).

It is worth remarking that the originally proposed dyotropic rearrangement, whether concerted or not [20], is unlikely, as evidence obtained from 2,3-dihalocholestanes indicates that diaxial-diequatorial rearrangement requires high temperatures (*ca.* 200°) [21]. Consequently, halogenation implicating the initial formation of a bridged bromonium ion could occur by backside attack of Cl-ion on either the secondary or tertiary termini to

Table 1. *Predictions of the Absolute Configuration of Halogenated Chamigrenes*

Reaction type	Halogenation of bisabolyl cation			Bisabolene intermediate	Trihalochamigrene product		
	Cation fixation	Cyclohexenyl configuration	Dyotropic shift	Configuration	Ring B tert. X	sec. X configuration	Relation of sec. Br. in ring A to sec. X in ring B
1-N	*si*	*S*	no	*E*	Br	*R*	*cis*
1-D			yes	*E*	Cl	*S*	*cis*
2-N	*si*	*R*	no	*Z*	Br	*S*	*trans*
2-D			yes	*Z*	Cl	*R*	*trans*
3-N	*re*	*S*	no	*Z*	Br	*R*	*trans*
3-D			yes	*Z*	Cl	*S*	*trans*
4-N	*re*	*R*	no	*E*	Br	*S*	*cis*
4-D			yes	*E*	Cl	*R*	*cis*

give, after elimination, **24** or **25** directly. As the exact nature of the mechanism is operationally immaterial, the formalism of a discrete dyotropic rearrangement is retained.

Accordingly, our two metabolites **12** and **13** must have arisen from a γ-bisabolyl cation having the (*R*)-configuration which was halogenated with dyotropic shift. In other words, the reaction type could have been 2-D or 4-D. Greater precision is not possible as the appropriater markers, the secondary Br-substituents in ring A, are missing. There is no means of knowing whether the bisabolyl cation, prior to halogenation, was fixed on its *si*- or *re*-face.

Even obtusol (**5**) and isoobtusol (**6**) do not conform to the originally proposed scheme [15] or reaction 1-N, because the ring-B chloromethine groups have the wrong, *i.e.* (*S*)-configurations. Their biogeneses must have occurred *via* reaction 4-N.

Glanduliferol (**29**), which contains an (*S*)-configured chloromethine group in ring B [22], is yet another exception to the original scheme, especially if chlorohydrin formation obeys the same stereoelectronic criteria as chlorobromination. Its genesis is explicable by reaction 4-N.

This modified biogenetic scheme should not only be more encompassing, but should encourage the search for metabolites accountable by the hitherto, less common reactions, *e.g.* 2-N, 2-D and 3-N, 3-D.

Experimental Part

General. M.p.: *Mitamura Riken* micro melting point apparatus. $[\alpha]_D$: *Atago AA-5* digital polarimeter. UV: *Jasco Uvidec 610* spectrometer. IR: *Hitachi* IR spectrophotometer *260-10*. ^{1}H-NMR: at 60 MHz on a *Jeol-JNM-PMX-60* and at 90 MHz on a *Jeol-FX-900* spectrometer. ^{13}C-NMR: at 22.5 MHz on the latter instrument. MS: electron-impact (EI) MS as well as high-resolution (HR) MS on a *Jeol-JMS-D-300* instrument.

Collection, Extraction, and Isolation. The sea hare *Aplysia dactylomela* was collected at Hisamatsu, Miyako, Okinawa, in April 1983. Six individuals (average weight 360 g) gave a total of 115 g of digestive glands which were homogenized and thoroughly extracted with acetone (2 × 500 ml). The extract was concentrated, and the resulting oil was successively extracted with hexane and AcOEt to give 3.8 and 1.4 g of crude oil, respectively. The oil extracted by hexane was separated on a silica-gel column with hexane/$CHCl_3$ 3:1 into five fractions *(A–E)*. Two prep. TLC separations (silica gel, hexane) of *Fraction A* gave **8** (3 mg) as slightly impure oil. *Fraction B* was chromatographed on a silica-gel column (hexane/acetone). An oily fraction eluted with acetone and showing an IR band at 2100 cm^{-1} was further purified on a TLC-grade silica-gel column (hexane/$CHCl_3$ 1:1) followed by prep. TLC (hexane/$CHCl_3$ 1:1) to yield **9** (50 mg). *Fraction C* was separated on a TLC-grade silica-gel column (hexane/$CHCl_3$ 1:3) into five fractions (*C-1* to *C-5*). *Fraction C-1* was again passed through the same column (hexane/AcOEt 10:1), and fractions giving a UV-active spot on TLC were collected and purified by running on a *Lobar-Si-60* column (hexane/AcOEt 5:1) to give **12** (38 mg) as light yellow glass. Crystallization from hexane/CCl_4 in a freezer gave colorless crystals, m.p. 98–100°. *Fraction C-2* was similarly separated on a TLC-grade silica-gel column (hexane/AcOEt 5:1) to yield a crystalline material which on recrystallization from MeOH gave **10** (32.3 mg) as colorless prisms, m.p. 97–99.5°. *Fraction C-4* was passed over a polystyrene column (MeOH) to remove greenish pigment. The resulting MeOH eluate (yellow oil) was separated on a silica-gel column (hexane/AcOEt 7:3) into 17 fractions. Fractions containing a UV-active spot were combined and run again on the same column with the same solvent to yield crystalline material. Recrystallization from hexane/$CHCl_3$ gave **13** (204 mg) as colorless crystals, m.p. 105–106°. The mother liquor gave more **13** (899 mg) as crude crystals.

Similar separation of a portion (630 mg) of the AcOEt extract furnished **9** (13.8 mg), **10** (22.6 mg), and **11** (30.6 mg). The latter was unstable and decomposed during storage in the freezer.

2,4-Dibromo-6-(2',4'-dibromophenoxy)anisole (**8**). Oil (3 mg); identical with the compound isolated from the green alga *Cladophora fascicularis* by TLC and ^{1}H-NMR. ^{1}H-NMR ($CDCl_3$): 7.77 (*d*, *J* = 2.4, 1 H); 7.48 (*d*, *J* = 2.1, 1 H); 7.37 (*dd*, *J* = 8.7, 2.4, 1 H); 6.90 (*d*, *J* = 2.1, 1 H); 6.73 (*d*, *J* = 8.7, 1 H); 3.88 (*s*, 3 H).

cis-*Maneonene C* (**9**). Colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.05 (*ddd*, *J* = 10.5, 9.5, 2.7, 1 H); 5.56 (*ddd*, *J* = 10.5, 3.7, 2.0, 1 H); 5.13 (*dd*, *J* = 4.9, 4.4, 1 H); 4.71 (*dd*, *J* = 10.8, 11.0, 1 H); 4.66 (*m*, 1 H); 4.28 (*dd*, *J* = 4.5, 4.4, 1 H); 3.45 (*dd*, *J* = 9.6, 4.4, 1 H); 3.29 (*d*, *J* = 2.4, 1 H); 2.68 (*m*, 2 H); 2.33 (*m*, 1 H); 1,90 (*m*, 1 H); 1.72 (*m*, 1 H); 1.12 (*t*, *J* = 7.0, 3 H). ^{13}C-NMR ($CDCl_3$): 141.6 (*d*), 110.3 (*d*), 104.9 (*s*), 85.2 (*s*), 83.5 (*d*), 80.9 (*d*), 78.0 (*d*), 54.2 (*d*), 53.6 (*d*), 44.5 (*d*), 36.3 (*t*), 27.4 (*t*), 13.2 (*q*). The ^{1}H-NMR data ($CDCl_3$) were somewhat different from that reported for *cis*-maneonene C in C_6D_6, while the ^{13}C-NMR data were virtually identical. MS (HR): 342.0030 ($C_{15}H_{16}{}^{79}Br^{35}ClO_2$, calc. 342.0023).

8-Bromo-9-chloro-5,5,9-trimethyl-1-methylidenespiro[5.5]undec-3-en-2-one (**12**). Colorless prisms, m.p. 98–100°, $[\alpha]_D$ = +19.6° (*c* = 0.64, $CHCl_3$). UV (EtOH): 235 (7300). IR (film): 2970, 1675, 1620, 1380, 1260, 1095, 845, 755. ^{1}H-NMR ($CDCl_3$): 6.51 (*d*, *J* = 10.1, 1 H); 6.15 (*s*, 1 H); 5.96 (*d*, *J* = 10.1, 0.4 H); 5.94 (*d*, *J* = 10.1, 0.6 H); 5.37 (*s*, 1 H); 4.67 (*dd*, *J* = 12.7, 5.0, 0.6 H); 4.25 (*dd*, *J* = 12.3, 4.5, 0.4 H); 1.68 (*s*, 3 H); 1.19 (*s*, 3 H); 1.04, 1.01 (2*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 190.4 (*s*), 158.0 (*d*), 126.4 (*d*), 122.1 (*t*) [121.6 (*t*)], 71.2 (*s*), 60.3 (*d*), 50.1 (*s*) [49.8 (*s*)], 41.8 (*s*), 38.9 (*t*) [38.6 (*t*)], 37.3 (*t*), 26.9 (*t*) [24.6 (*t*)], 23.9 (*q*), 23.5 (*q*), 22.5 (*q*). EI-MS: 334 (5.5), 332 (21), 330 (16), 319 (0.9), 317 (3.4), 315 (2.6), 297 (2.6), 295 (2.7), 253 (12), 251 (35), 215 (72), 214 (17), 199 (54), 119 (30), 117 (20), 105 (32), 96 (100), 91 (37), 81 (41), 77 (29), 67 (36), 53 (42). MS (HR): 330.0406 ($C_{15}H_{20}{}^{79}Br^{35}ClO$, calc. 330.0386).

4-Bromo-3-chloro-3,7,7-trimethyl-10-oxospiro[5.5]undec-8-en-1-yl Acetate (**13**). Colorless prisms, m.p. 105–106°, $[\alpha]_D^{20}$ = −27.8° (*c* = 0.54, $CHCl_3$). UV (EtOH): 235 (6600): IR (KBr): 2970, 1735, 1678, 1610, 1370, 1235, 1040, 1020, 940, 842. ^{1}H-NMR ($CDCl_3$): 6.40 (*d*, *J* = 10.1, 1 H); 6.30 (*s*, 1 H); 5.93 (*d*, *J* = 10.1, 1 H); 5.55 (br. *s*, 1 H); 5.29 (*t*, *J* = 8, 1 H); 4.65 (*dd*, *J* = 13.0, 5.3, 1 H); 2.58 (*dd*, *J* = 14.7, 5.1, 1 H); 2.07 (*dd*, *J* = 14.7, 13, 1 H); 1.90 (*s*, 3 H); 1.75 (*s*, 3 H); 1.10 (*s*, 3 H); 1.02 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 189.0 (*s*), 168.4 (*s*), 155.9 (*d*), 144.5 (*s*), 125.9 (*d*), 123.3 (*t*), 69.4 (*d*), 68.8 (*s*), 58.6 (*d*), 52.7 (*s*), 43.3 (*t*), 40.5 (*s*), 37.4 (*t*), 24.7 (*q*), 24.1 (*q*), 22.0 (*q*), 20.8 (*q*). EI-MS: 392 (3), 390 (10), 388 (7), 350 (15), 348 (56), 346 (44), 333 (5), 331 (13), 329 (9), 332 (5.5), 330 (14), 328 (10),

Table 2. *Crystal Data, Intensity Measurement, and Structure Refinement*

	12	**17**
Formula	$C_{15}H_{20}BrClO$	$C_{15}H_{20}BrClO_2$
Molecular weight	331.7	347.7
Crystal system	Monoclinic	Orthorhombic
Space group	$P2_1$	$P2_12_12_1$
Crystal size [mm]	0.18 × 0.25 × 0.28	0.15 × 0.23 × 0.35
Unit cell determination	Least-squares fit from 27 refl. ($29° \leq 2\theta \leq 36°$)	Least-squares fit from 23 refl. ($22° \leq 2\theta \leq 31°$)
a [Å]	7.4921(15)	9.267(1)
b [Å]	10.621(3)	14.211(4)
c [Å]	10.267(2)	23.025(7)
β [°]	110.44(1)	90.0
Z	2	8
D_{calc} [g cm^{-3}]	1.439	1.523
F_{000}	340	1424
μ [cm^{-1}]	28.21	28.57
$(\sin\theta/\lambda)_{max}$ [Å^{-1}]	0.62	0.53
h,k,l Range	−8.8 0.13 0.12 and all antireflections of these	0.9 0.15 0.20 and all antireflections of these
Number of *Friedel* pairs measured	1510	1637
Criterion for observed reflections	$\|F\| \geq 3\sigma(F)$ and $\|F\| \geq 7$	$\|F\| \geq 3\sigma(F)$ and $\|F\| \geq 8$
Number of observed reflections	1390	2637
Refinement	full-matrix	two blocks
Number of parameters	163	345
Weighting scheme	$w(F) = \exp(18 \cdot (\sin\theta/\lambda)^2)$	$w(F) = (\|F\|/48)^2$ for $\|F\| \leq 48$ and $(48/\|F\|)^2$ for $\|F\| \geq 48$
Coordinates of H-atoms	calculated	calculated
Max and min $\Delta\rho$ [eÅ^{-3}]	0.40, −0.73	0.77, −0.79
R, w*R* [%]	3.8, 4.6	7.4, 9.8
Absolute-structure parameter [7]	−0.01(2)	0.06(2)

249 (24), 231 (34), 213 (52), 187 (45), 117 (32), 149 (31), 137 (23), 135 (> 100), 105 (34), 96 (100), 91 (49), 81 (36), 69 (49). MS (HR): 390.0434 ($C_{17}H_{22}{}^{81}Br^{35}ClO_3$, calc. 390.0422).

9-((Z)-Bromomethylidene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (**10**). Colorless prisms, m.p. 97–99.5°, $[\alpha]_D^{20} = +33.5°$ ($c = 0.074$, $CHCl_3$). UV (EtOH): 253 (27000). IR (KBr): 2930, 1645, 1605, 1365, 1330, 1325, 1300, 940, 765. ^{1}H-NMR ($CDCl_3$): 6.78 (*dd*, $J = 10.2, 1.0$, 1 H); 6.01 (*dd*, $J = 1.5, 1.1$, 1 H); 5.62 (*dd*, $J = 10.1, 1.5$, 1 H); 1.85 (*d*, $J = 1.1$, 3 H); 1.77 (*d*, $J = 0.9$, 3 H); 0.97 (*d*, $J = 6.4$, 3 H). ^{13}C-NMR ($CDCl_3$): 197.8 (*s*), 159.9 (*s*), 138.6 (*d*), 136.4 (*s*), 131.4 (*s*), 127.4 (*d*), 102.8 (*d*), 45.8 (*s*), 41.2 (*t*), 38.0 (*d*), 28.3 (*t*), 26.2 (*t*), 19.4 (*q*), 17.4 (*q*), 11.8 (*q*). EI-MS: 296 (48), 294 (48), 281 (8), 279 (8), 254 (54), 252 (56), 239 (29), 237 (30), 227 (52), 225 (60), 215 (**48**), 173 (100), 158 (38), 145 (69), 130 (29), 129 (42), 128 (34), 125 (22), 117 (26), 115 (40), 105 (24), 91 (64), 77 (33), 71 (33), 65 (27), 53 (27), 51 (23). MS (HR): 294.0624 ($C_{15}H_{19}{}^{79}BrO$, calc. 294.0621).

9-((E)-Bromomethylidene)-1,2,5-trimethylspiro[5.5]undeca-1,7-dien-3-one (**11**). Colorless oil; ^{1}H-NMR ($CDCl_3$): 6.35 (*dd*, $J = 10.1, 0.5$, 1 H); 6.23 (*m*, 1 H); 5.45 (*d*, $J = 9.9$, 1 H); 1.84 (*d*, $J = 0.9$, 3 H); 1.77 (*d*, $J = 0.9$, 3 H); 0.97 (*d*, $J = 6.4$, 3 H). EI-MS: 296 (56), 294 (63), 281 (13), 279 (13), 254 (58), 252 (61), 239 (31), 237 (35), 227 (66), 225 (73), 215 (58), 173 (100), 158 (34), 145 (59), 130 (22), 128 (24), 91 (52). MS (HR): 296.0601 ($C_{15}H_{19}{}^{81}BrO$, calc. 296.0600).

Saponification of **13**. A soln. of **13** (81.0 mg) in 2 ml of 1% KOH in 95% EtOH was allowed to stand at r.t. for 30 min. The soln. was acidified with HCl/EtOH to pH 4, concentrated, and separated on a short silica-gel column ($CHCl_3$) to give *10-bromo-9-chloro-7-hydroxy-5,5,9-trimethyl-1-methylidenespiro[5.5]undec-3-en-2-one* (**16**; 21.8 mg, 31.7%) and *10-bromo-9-chloro-4,7-epoxy-5,5,9-trimethyl-1-methylidenespiro[5.5]undecan-2-one* (**17**; 47.3 mg, 65.8%). Alcohol **16** was recrystallized from hexane/$CHCl_3$ to give colorless needles, m.p. 174–176°. IR (KBr): 3300 (br.), 2920, 1660, 1605, 1450, 1400, 1375, 1310, 1270, 1100, 1040, 1010, 975, 950, 835. ^{1}H-NMR ($CDCl_3$): 6.46 (*d*, $J = 10.0$, 1 H); 6.18 (*s*, 1 H); 5.93 (*d*, $J = 10.0$, 1 H); 5.40 (*s*, 1 H); 4.63 (*dd*, $J = 13.0, 5.0$, 1 H); 4.11 (*t*, $J = 8.0$, 1 H); 2.53 (*dd*, $J = 14.0, 5.0$, 1 H); 2.66 (*d*, $J = 8.0$, 1 H); 2.00 (*dd*, $J = 14.0, 13.0$, 1 H); 1.73 (*s*, 3 H); 1.28 (*s*, 3 H); 1.03 (*s*, 3 H). EI-MS: 350, 348 (1), 346 (0.8), 313 (0.6), 269 (0.7), 267 (2), 251 (0.7), 249 (1), 241 (0.8), 239 (2.5), 231 (3.6), 215 (1.3), 213 (3.5), 203 (2.3), 187 (6.6), 175 (2), 173 (2.3), 163 (3), 149 (7), 137 (9), 136 (14), 135 (100), 96 (11), 91 (10), 77 (62), 67 (10). MS (HR): 348.0333 ($C_{15}H_{20}{}^{81}Br^{35}ClO_2$, calc. 348.0316).

Ether **17** was recrystallized from hexane/$CHCl_3$ to give colorless prisms, m.p. 144–145°. UV (EtOH): 225 (4150). IR (KBr): 2910, 1690, 1600, 1390, 1205, 1140, 1120, 1095, 1040, 1000, 960, 865, 805, 790. ^{1}H-NMR ($CDCl_3$): 6.20 (*s*, 1 H); 5.30 (*s*, 1 H); 4.57 (*dd*, $J = 13.0, 5.0$, 1 H); 4.06 (*m*, 2 H); 1.75 (*s*, 3 H); 1.27 (*s*, 3 H); 1.00 (*s*, 3 H).

Acid Treatment of **16**. A soln. of **16** (24.4 mg) and TsOH (2.1 mg) in benzene (2 ml) was heated at reflux for 3 h. The mixture was poured onto a small silica-gel column and eluted with $CHCl_3$ to yield 21.6 mg (88.5%) of **17**, m.p. 144–145°.

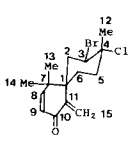
Table 3. *Fractional Coordinates and Equivalent Isotropic Temperature Factors,* U_{eq} ($\times 10^3 A^2$) *with e.s.d.'s in Parentheses for* **12** *and* **17**[a])

	Atom	*x*	*y*	*z*	U_{eq}
12	Br	0.25062(16)	0.2178	−0.12451(5)	87.8(4)
	Cl	−0.0718(4)	0.0457(4)	−0.01822(24)	90.6(10)
	O	0.2826(10)	0.2467(9)	0.5776(5)	75(3)
	C(1)	0.4927(9)	0.1694(8)	0.3180(5)	41(3)
	C(2)	0.4573(9)	0.2065(14)	0.1637(5)	53(3)
	C(3)	0.2543(11)	0.1746(8)	0.0638(5)	49(3)
	C(4)	0.1893(13)	0.0437(10)	0.0737(6)	54(3)
	C(5)	0.2155(11)	0.0183(8)	0.2262(6)	46(3)
	C(6)	0.4252(10)	0.0324(9)	0.3181(5)	43(3)
	C(7)	0.7124(11)	0.1830(12)	0.4082(7)	60(4)
	C(8)	0.7332(10)	0.1707(9)	0.5610(6)	53(3)
	C(9)	0.6014(11)	0.1861(8)	0.6163(5)	54(3)
	C(10)	0.4065(10)	0.2315(10)	0.5303(4)	45(3)
	C(11)	0.3819(9)	0.2532(7)	0.3793(4)	39(3)
	C(12)	0.2692(23)	−0.0575(14)	0.0105(10)	95(6)
	C(13)	0.8371(16)	0.0825(16)	0.3785(12)	83(5)
	C(14)	0.7837(17)	0.3159(15)	0.3920(13)	83(5)
	C(15)	0.2771(13)	0.3541(9)	0.3260(6)	58(3)

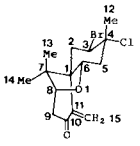
Table 3 (cont.)

	Atom	*x*	*y*	*z*	U_{eq}
17i	Br(1)	0.64372(12)	0.44413(11)	0.20165(8)	67.3(5)
	Cl(1)	0.4056(3)	0.61273(21)	0.25530(17)	54.1(10)
	O(1)	−0.0031(6)	0.3841(5)	0.1971(3)	36.0(23)
	O(2)	0.0342(9)	0.3414(7)	0.3500(4)	52(3)
	C(1)	0.2265(10)	0.3230(8)	0.2140(5)	33(4)
	C(2)	0.3852(11)	0.3359(7)	0.1982(5)	37(3)
	C(3)	0.4395(9)	0.4310(7)	0.2215(5)	28(3)
	C(4)	0.3505(12)	0.5133(7)	0.2057(5)	34(3)
	C(5)	0.1875(10)	0.4967(8)	0.2228(6)	39(4)
	C(6)	0.1440(11)	0.4096(6)	0.1918(5)	30(3)
	C(7)	0.1323(10)	0.2443(6)	0.1845(4)	29(3)
	C(8)	−0.0165(12)	0.2836(7)	0.2049(5)	30(3)
	C(9)	−0.0533(10)	0.2670(8)	0.2650(6)	43(4)
	C(10)	0.0562(11)	0.3120(8)	0.3033(5)	31(4)
	C(11)	0.2139(10)	0.3102(6)	0.2782(5)	31(4)
	C(12)	0.3644(19)	0.5526(11)	0.1458(5)	60(5)
	C(13)	0.1489(12)	0.2430(8)	0.1213(5)	46(4)
	C(14)	0.1599(12)	0.1451(8)	0.2076(6)	48(4)
	C(15)	0.3126(16)	0.2868(9)	0.3159(7)	57(5)
17ii	Br(101)	0.36683(14)	0.73814(7)	0.41947(7)	58.2(4)
	Cl(101)	0.1100(3)	0.61403(23)	0.49694(16)	51.6(9)
	O(101)	0.4400(8)	0.3226(6)	0.4697(5)	55(3)
	O(102)	0.5316(16)	0.3948(8)	0.6210(5)	76(5)
	C(101)	0.5430(8)	0.4754(7)	0.4699(5)	28(4)
	C(102)	0.5275(10)	0.5737(8)	0.4392(5)	37(3)
	C(103)	0.3860(12)	0.6156(7)	0.4604(5)	35(3)
	C(104)	0.2493(10)	0.5557(8)	0.4544(6)	36(4)
	C(105)	0.2766(11)	0.4589(8)	0.4797(6)	45(4)
	C(106)	0.4091(13)	0.4190(8)	0.4545(6)	41(4)
	C(107)	0.6601(11)	0.4019(8)	0.4451(6)	37(4)
	C(108)	0.6007(10)	0.3179(8)	0.4740(6)	37(4)
	C(109)	0.6207(13)	0.3089(8)	0.5390(5)	43(4)
	C(110)	0.5661(13)	0.3936(10)	0.5692(6)	51(5)
	C(111)	0.5642(10)	0.4816(8)	0.5343(5)	33(4)
	C(112)	0.1950(15)	0.5492(10)	0.3928(6)	53(4)
	C(113)	0.6630(13)	0.3934(11)	0.3818(5)	53(5)
	C(114)	0.8158(11)	0.4295(12)	0.4673(8)	68(5)
	C(115)	0.6010(10)	0.5607(8)	0.5611(6)	45(4)

[a]) Numbering:



12



17

Oxidation of **16**. To a soln. of **16** (22.9 mg) in acetone (2 ml) was added a few drops of *Jones* reagent, and the mixture was stirred at r.t. for 10 min and directly poured onto a short silica-gel column to give *4-bromo-3-chloro-3,11,11-trimethyl-7-methylidenespiro[5.5]undec-9-ene-1,8-dione* (**18**; 15.7 mg, 68.2%). Recrystallization from hexane/$CHCl_3$ gave **18** as colorless, fine needles, m.p. 122–129°. UV (EtOH): 203 (6080), 225 (4890). IR ($CHCl_3$): 2960, 1720, 1670, 1605, 1460, 1400, 1380, 1270, 1120, 1075, 1040, 950, 840. ^{1}H-NMR ($CDCl_3$): 6.87 (*d*, *J* = 10.0, 1

H); 6.07 (*s*, 1 H); 5.90 (*d*, *J* = 10.0, 1 H); 5.73 (*s*, 1 H); 4.93 (*dd*, *J* = 13.0, 5.0, 1 H); 1.60 (*s*, 3 H); 1.25 (*s*, 3 H); 1.02 (*s*, 3 H). EI-MS: 348 (3), 346 (9), 344 (8), 333 (8), 331 (29), 329 (23), 267 (5), 265 (13), 229 (23), 201 (23), 187 (22), 175 (11), 173 (12), 163 (23), 161 (10), 159 (15), 135 (100), 121 (24), 105 (31), 96 (28), 91 (36), 77 (23), 67 (33), 53 (36). MS (HR): 348.0101 ($C_{15}H_{18}{}^{81}Br^{37}ClO_2$, calc. 348.0127).

Treatment of **18** *with 0.1% KOH/EtOH.* A soln. of **18** (37.3 mg) in 0.1% KOH in 95% EtOH (2 ml) was allowed to stand at r.t. for 1 h. The soln. was acidified with HCl/EtOH to pH 4, concentrated, and separated on a *Lobar-Si-60* column ($CHCl_3$) to give *4-bromo-3,11,11-trimethyl-7-methylidenespiro[5.5]undeca-2,9-diene-1,8-dione* (**19**; 24.3 mg, 72.8%) as colorless crystals, after recrystallization from hexane/$CHCl_3$, m.p. 119–120°. UV (EtOH): 237 (8660). IR (KBr): 2950, 1660, 1615, 1400, 1375, 1305, 1285, 1250, 1210, 1160, 1120, 850, 775. ^{1}H-NMR ($CDCl_3$): 6.65 (*d*, *J* = 10.1, 1 H); 6.11 (*s*, 1 H); 6.00 (*d*, *J* = 10.1, 1 H); 5.95 (br. *s*, 1 H); 5.16 (*s*, 1 H); 4.70 (*dd*, *J* = 10.8, 5.2, 1 H); 2.93 (*dd*, *J* = 13.7, 5.2, 1 H); 2.63 (*dd*, *J* = 13.7, 10.8, 1 H); 2.09 (br. *s*, 3 H); 1.43 (*s*, 3 H); 1.19 (*s*, 3 H). EI-MS: 310 (2), 308 (2), 295 (6), 293 (7), 267 (5), 230 (18), 229 (65), 215 (13), 213 (21), 211 (19), 202 (15), 201 (75), 187 (40), 121 (100), 91 (38), 77 (38), 67 (34), 53 (36).

Treatment of **18** *with 0.5% KOH/EtOH.* A soln. of **18** (16.3 mg) in 0.5% KOH in 95% EtOH (2 ml) was allowed to stand at r.t. for 12 min. The mixture was acidified with HCl/EtOH to pH 4, concentrated, and separated by TLC (silica gel, hexane/$CHCl_3$ 1:2) to furnish 7.5 mg (51.7%) of *8-bromo-2,2,9-trimethyltricyclo[6.3.1.0^{1,6}]dodeca-3,9-diene-5,11-dione* (**20**) as colorless needles, after recrystallization from hexane/$CHCl_3$, m.p. 124.5–127°. UV (EtOH): 233 (8700). IR (KBr): 2930, 1660, 1620, 1460, 1370, 1270, 1215, 1120, 1075, 940, 870, 805. ^{1}H-NMR ($CDCl_3$): 6.71 (*d*, *J* = 9.9, 1 H); 5.92 (*d*, *J* = 9.9, 1 H); 5.72 (*q*, *J* = 1.3, 1 H); 2.67 (*s*, 2 H); 2.17 (*d*, *J* = 1.3, 3 H); 1.48 (*s*, 3 H); 1.23 (*s*, 3 H). EI-MS: 310 (31), 308 (32), 229 (100), 215 (17), 213 (38), 211 (48), 201 (47), 185 (21), 159 (26), 121 (39), 93 (23), 91 (34), 79 (29), 77 (35), 69 (56), 65 (27), 55 (30). MS (HR): 308.0397 ($C_{15}H_{17}{}^{79}BrO_2$, calc. 308.0410).

Table 4. *Bond Distances, Bond Angles, and Torsion Angles for* **12** *and* **17**

Interatomic distances [Å] of **12** with e.s.d.'s in parentheses			
Br–C(3)	1.978(6)	C(4)–C(12)	1.485(19)
Cl–C(4)	1.852(9)	C(5)–C(6)	1.531(9)
O–C(10)	1.199(11)	C(7)–C(8)	1.527(10)
C(1)–C(2)	1.563(8)	C(7)–C(13)	1.519(19)
C(1)–C(6)	1.541(12)	C(7)–C(14)	1.540(20)
C(1)–C(7)	1.588(9)	C(8)–C(9)	1.310(12)
C(1)–C(11)	1.498(10)	C(9)–C(10)	1.497(10)
C(2)–C(3)	1.546(9)	C(10)–C(11)	1.514(7)
C(3)–C(4)	1.489(13)	C(11)–C(15)	1.328(12)
C(4)–C(5)	1.532(10)		
Bond angles [°] of **12** with e.s.d.'s in parentheses			
C(2)–C(1)–C(6)	107.4(7)	C(4)–C(5)–C(6)	110.5(7)
C(2)–C(1)–C(7)	110.1(6)	C(1)–C(6)–C(5)	111.0(6)
C(2)–C(1)–C(11)	110.7(6)	C(1)–C(7)–C(8)	107.8(7)
C(6)–C(1)–C(7)	111.0(7)	C(1)–C(7)–C(13)	113.7(8)
C(6)–C(1)–C(11)	109.3(6)	C(1)–C(7)–C(14)	110.4(8)
C(7)–C(1)–C(11)	108.3(6)	C(8)–C(7)–C(13)	107.3(8)
C(1)–C(2)–C(3)	113.4(7)	C(8)–C(7)–C(14)	106.0(8)
Br–C(3)–C(2)	105.8(5)	C(13)–C(7)–C(14)	111.2(10)
Br–C(3)–C(4)	113.0(4)	C(7)–C(8)–C(9)	127.8(6)
C(2)–C(3)–C(4)	115.4(7)	C(8)–C(9)–C(10)	120.8(5)
Cl–C(4)–C(3)	105.5(6)	O–C(10)–C(9)	122.5(5)
Cl–C(4)–C(5)	105.0(6)	O–C(10)–C(11)	124.0(6)
Cl–C(4)–C(12)	107.5(7)	C(9)–C(10)–C(11)	113.5(6)
C(3)–C(4)–C(5)	107.8(6)	C(1)–C(11)–C(10)	116.9(6)
C(3)–C(4)–C(12)	117.0(10)	C(1)–C(11)–C(15)	129.9(6)
C(5)–C(4)–C(12)	113.1(8)	C(10)–C(11)–C(15)	112.9(7)

Table 4 (cont.)

Torsion angles [°] of **12** with e.s.d.'s in parentheses

C(6)–C(1)–C(2)–C(3)	49.2(10)	C(1)–C(2)–C(3)–C(4)	– 50.1(11)
C(7)–C(1)–C(2)–C(3)	170.2(9)	Br–C(3)–C(4)–Cl	– 73.2(6)
C(11)–C(1)–C(2)–C(3)	– 70.1(11)	Br–C(3)–C(4)–C(5)	175.1(6)
C(2)–C(1)–C(6)–C(5)	– 57.2(8)	Br–C(3)–C(4)–C(12)	46.3(8)
C(7)–C(1)–C(6)–C(5)	–177.6(6)	C(2)–C(3)–C(4)–Cl	164.9(5)
C(11)–C(1)–C(6)–C(5)	62.9(6)	C(2)–C(3)–C(4)–C(5)	53.1(9)
C(2)–C(1)–C(7)–C(8)	169.2(9)	C(2)–C(3)–C(4)–C(12)	– 75.7(8)
C(2)–C(1)–C(7)–C(13)	– 71.9(12)	Cl–C(4)–C(5)–C(6)	–172.1(6)
C(2)–C(1)–C(7)–C(14)	54.0(11)	C(3)–C(4)–C(5)–C(6)	– 60.0(9)
C(6)–C(1)–C(7)–C(8)	– 72.0(9)	C(12)–C(4)–C(5)–C(6)	71.0(11)
C(6)–C(1)–C(7)–C(13)	46.9(10)	C(4)–C(5)–C(6)–C(1)	65.1(8)
C(6)–C(1)–C(7)–C(14)	172.8(8)	C(1)–C(7)–C(8)–C(9)	– 20.1(14)
C(11)–C(1)–C(7)–C(8)	48.1(10)	C(13)–C(7)–C(8)–C(9)	–143.1(10)
C(11)–C(1)–C(7)–C(13)	166.9(8)	C(14)–C(7)–C(8)–C(9)	98.1(11)
C(11)–C(1)–C(7)–C(14)	– 67.2(9)	C(7)–C(8)–C(9)–C(10)	– 5.7(15)
C(2)–C(1)–C(11)–C(10)	–178.1(7)	C(8)–C(9)–C(10)–O	180.0(9)
C(2)–C(1)–C(11)–C(15)	– 5.7(11)	C(8)–C(9)–C(10)–C(11)	1.2(13)
C(6)–C(1)–C(11)–C(10)	63.8(7)	O–C(10)–C(11)–C(1)	–146.8(10)
C(6)–C(1)–C(11)–C(15)	–123.9(8)	O–C(10)–C(11)–C(15)	39.6(14)
C(7)–C(1)–C(11)–C(10)	– 57.3(9)	C(9)–C(10)–C(11)–C(1)	32.1(11)
C(7)–C(1)–C(11)–C(15)	115.0(9)	C(9)–C(10)–C(11)–C(15)	–141.6(8)
C(1)–C(2)–C(3)–Br	–175.8(7)		

Interatomic distances [Å] (average standard deviation = 0.015 Å)

	17i[a])	**17ii**[a])		**17i**[a])	**17ii**[a])
Br(1)–C(3)	1.956	1.989	C(4)–C(5)	1.578	1.516
Cl(1)–C(4)	1.873	1.820	C(4)–C(12)	1.494	1.507
O(1)–C(6)	1.416	1.444	C(5)–C(6)	1.484	1.472
O(1)–C(8)	1.445	1.494	C(7)–C(8)	1.560	1.474
O(2)–C(10)	1.172	1.234	C(7)–C(13)	1.463	1.464
C(1)–C(2)	1.526	1.573	C(7)–C(14)	1.528	1.581
C(1)–C(6)	1.536	1.518	C(8)–C(9)	1.445	1.512
C(1)–C(7)	1.573	1.610	C(9)–C(10)	1.489	1.480
C(1)–C(11)	1.495	1.499	C(10)–C(11)	1.572	1.487
C(2)–C(3)	1.538	1.521	C(11)–C(15)	1.303	1.327
C(3)–C(4)	1.476	1.532			

Bond angles [°] (average standard deviation = 0.9°)

	17i[a])	**17ii**[a])		**17i**[a])	**17ii**[a])
C(6)–O(1)–C(8)	110.3	104.8	Cl(1)–C(4)–C(5)	102.7	108.9
C(2)–C(1)–C(6)	107.7	106.8	Cl(1)–C(4)–C(12)	104.8	107.3
C(2)–C(1)–C(7)	121.1	118.6	C(3)–C(4)–C(5)	110.8	109.3
C(2)–C(1)–C(11)	109.0	113.9	C(3)–C(4)–C(12)	118.3	113.3
C(6)–C(1)–C(7)	98.6	97.2	C(5)–C(4)–C(12)	111.7	111.2
C(6)–C(1)–C(11)	112.8	111.6	C(4)–C(5)–C(6)	105.4	109.7
C(7)–C(1)–C(11)	107.3	107.5	O(1)–C(6)–C(1)	104.2	106.4
C(1)–C(2)–C(3)	109.7	106.4	O(1)–C(6)–C(5)	115.7	115.8
Br(1)–C(3)–C(2)	108.6	105.5	C(1)–C(6)–C(5)	111.9	112.8
Br(1)–C(3)–C(4)	114.1	111.7	C(1)–C(7)–C(8)	96.1	96.5
C(2)–C(3)–C(4)	115.3	117.8	C(1)–C(7)–C(13)	112.3	114.8
Cl(1)–C(4)–C(3)	107.1	106.5	C(1)–C(7)–C(14)	114.4	109.9

Table 4 (cont.)

Torsional angles [°] (average standard deviation = 1.0°)

	17i	17ii		17i	17ii
C(8)–C(7)–C(13)	113.3	112.9	O(2)–C(10)–C(9)	125.4	123.7
C(8)–C(7)–C(14)	112.0	113.3	O(2)–C(10)–C(11)	120.3	120.5
C(13)–C(7)–C(14)	108.4	109.0	C(9)–C(10)–C(11)	114.2	115.7
O(1)–C(8)–C(7)	103.9	107.8	C(1)–C(11)–C(10)	115.7	119.1
O(1)–C(8)–C(9)	107.6	101.1	C(1)–C(11)–C(15)	129.4	122.9
C(7)–C(8)–C(9)	116.0	118.0	C(10)–C(11)–C(15)	114.4	117.3
C(8)–C(9)–C(10)	109.6	110.8			

Torsional angles [°] (average standard deviation = 1.0°)

	17i	17ii		17i	17ii
C(8)–O(1)–C(6)–C(1)	– 15.6	– 18.6	C(1)–C(2)–C(3)–Br(1)	179.0	–178.6
C(8)–O(1)–C(6)–C(5)	–138.9	–144.8	C(1)–C(2)–C(3)–C(4)	– 51.6	– 53.2
C(6)–O(1)–C(8)–C(7)	– 17.5	– 16.3	Br(1)–C(3)–C(4)–Cl(1)	– 69.0	– 69.5
C(6)–O(1)–C(8)–C(9)	106.0	108.1	Br(1)–C(3)–C(4)–C(5)	179.7	172.9
C(6)–C(1)–C(2)–C(3)	54.0	56.7	Br(1)–C(3)–C(4)–C(12)	48.9	48.3
C(7)–C(1)–C(2)–C(3)	166.1	165.0	C(2)–C(3)–C(4)–Cl(1)	164.3	168.2
C(11)–C(1)–C(2)–C(3)	– 68.8	– 67.0	C(2)–C(3)–C(4)–C(5)	53.0	50.6
C(2)–C(1)–C(6)–O(1)	168.3	165.5	C(2)–C(3)–C(4)–C(12)	– 77.8	– 74.0
C(2)–C(1)–C(6)–C(5)	– 65.9	– 66.5	Cl(1)–C(4)–C(5)–C(6)	–171.6	–167.7
C(7)–C(1)–C(6)–O(1)	41.6	42.7	C(3)–C(4)–C(5)–C(6)	– 57.5	– 51.6
C(7)–C(1)–C(6)–C(5)	167.4	170.7	C(12)–C(4)–C(5)–C(6)	76.7	74.3
C(11)–C(1)–C(6)–O(1)	– 71.3	– 69.4	C(4)–C(5)–C(6)–O(1)	–175.4	–173.3
C(11)–C(1)–C(6)–C(5)	54.5	58.6	C(4)–C(5)–C(6)–C(1)	65.4	63.8
C(2)–C(1)–C(7)–C(8)	–166.0	–163.0	C(1)–C(7)–C(8)–O(1)	41.5	41.2
C(2)–C(1)–C(7)–C(13)	– 47.7	– 44.0	C(1)–C(7)–C(8)–C(9)	– 76.3	– 72.3
C(2)–C(1)–C(7)–C(14)	76.5	79.2	C(13)–C(7)–C(8)–O(1)	– 76.0	– 79.3
C(6)–C(1)–C(7)–C(8)	– 49.2	– 49.4	C(13)–C(7)–C(8)–C(9)	166.2	167.2
C(6)–C(1)–C(7)–C(13)	69.2	69.6	C(14)–C(7)–C(8)–O(1)	161.0	156.2
C(6)–C(1)–C(7)–C(14)	–166.6	–167.1	C(14)–C(7)–C(8)–C(9)	43.2	42.7
C(11)–C(1)–C(7)–C(8)	68.1	66.1	O(1)–C(8)–C(9)–C(10)	– 55.3	– 63.2
C(11)–C(1)–C(7)–C(13)	–173.6	–174.9	C(7)–C(8)–C(9)–C(10)	60.5	54.0
C(11)–C(1)–C(7)–C(14)	– 49.4	– 51.7	C(8)–C(9)–C(10)–O(2)	150.3	158.7
C(2)–C(1)–C(11)–C(10)	170.7	174.2	C(8)–C(9)–C(10)–C(11)	– 34.8	– 25.4
C(2)–C(1)–C(11)–C(15)	– 18.3	– 15.4	O(2)–C(10)–C(11)–C(1)	–148.0	–153.8
C(6)–C(1)–C(11)–C(10)	51.0	53.1	O(2)–C(10)–C(11)–C(15)	39.7	35.1
C(6)–C(1)–C(11)–C(15)	–138.0	–136.4	C(9)–C(10)–C(11)–C(1)	36.8	30.2
C(7)–C(1)–C(11)–C(10)	– 56.5	– 52.4	C(9)–C(10)–C(11)–C(15)	–135.5	–140.9
C(7)–C(1)–C(11)–C(15)	114.5	118.1			

[a]) **i** and **ii** are the 2 molecules of the asymetric unit of **17**.

Conversion of **19** *to* **20**. A soln. of **19** (2.8 mg) in 0.5% KOH/EtOH was similarly treated as above, and the product mixture was separated in the same manner to give a small amount of **20**. Its IR was identical with that of **20** obtained directly from **18** using the same base.

Isomerization of **10** *to* **11**. When a soln. of **10** in $CHCl_3$ was allowed to stand at r.t., it spontaneously transformed into an oily substance which was shown to be identical with **11** by TLC and IR.

Crystallographic Data for **12** *and* **17**. The lattice parameters and diffracted intensities were measured at r.t. on an automatic four-circle *Philips PW 1100* diffractometer using graphite-monochromated MoK_α radiation. No absorption correction was applied. The structures were solved by direct methods [23]. All calculations were performed with a local version of XRAY-76 [24].

Exper. data and structure refinement are summarized in *Table 2*. The absolute configurations of **12** and **17** were confirmed by least-squares refinement of the absolute-structure parameter [7]. Compound **17** crystallizes with 2 molecules per asymmetric unit. These 2 molecules (**i** and **ii**) have the same configuration and reveal no quantifiable differences in their individual conformations (see *Table 4*). The positional and vibrational parameters (*Table 3*) as well as the bond lengths, bond angles, and torsional angles were determined (*Table 4*).

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