Photo-induced Transformations. Part 57.[1] The Formation of Bridged Oxabicyclic Compounds by Intramolecular Radical Addition of Oxyl Radicals Generated from Some A-Homo-4a-cholesten-3-ol Hypoiodites

By **Hiroshi Suginome,*** Organic Synthesis Division, Department of Chemical Process Engineering, Faculty of Engineering and Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060, Japan
Shigeru Isayama, Norio Maeda, and **Akio Furusaki,** Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060, Japan
(in part) **Chuji Katayama,** Department of Chemistry, Faculty of Science, Nagoya University, Chikusaku Nagoya 464, Japan

Photoinduced reaction of the hypoiodites of A-homo-4a-cholesten-3α- and -3β-ol resulted in the formation of 3α,5-epoxy-4aβ-iodo-A-homo-5β-cholestane and 3β,5-epoxy-4aα-iodo-A-homo-5α-cholestane, respectively. 3α-Methyl-A-homo-4a-cholesten-3β-ol and the 3α isomer likewise gave 3β,5-epoxy-3α-methyl-4aβ-iodo-A-homo-5α-cholestane and 3α,5-epoxy-3β-methyl-4aα-iodo-A-homo-5β-cholestane, respectively, in good yield. Thus, unlike the corresponding reaction of 5-cholesten-3-ols, the intramolecular radical addition is a faster process than the β-cleavage in the oxyl radical derived from A-homo-4a-cholesten-3-ols.

IN previous papers [2-4] the photo- and thermally-induced radical rearrangements of the hypoiodites of cholesterol and several related 5-cholesten-3-ols with the methyl groups at C-3 or C-4 in the presence of mercury(II) oxide and iodine were reported. It has been found that regardless of whether it was induced photochemically or thermally, 3α,5-epoxy-A-homo-4-oxa-5α-cholestanes bearing a 6α- or 6β-iodine or 3α,5-epoxy-A-homo-4-oxa-5α-cholest-6-enes are the common products. Methyl substituents at C-3 or C-4, however, appreciably affected the relative yields of the products. Notably, introduction of two methyl groups at C-4 of 5-cholesten-3-ols led to the additional formation of 3-oxa-5-cholestenes. It has also been found [5] that changing the steroid C-ring from six-membered to five-membered causes appreciable variations in the products and their yields. Probable reaction paths involving allyl radical intermediates which rationalize the type of the products, as well as their stereochemistry, have been proposed.

In this paper, the results of a study of the photo-induced reactions of hypoiodites of some steroidal seven-membered cyclic homoallyl alcohols, A-homo-4a-cholesten-3-ols, in the presence of mercury(II) oxide and iodine, are reported.

RESULTS AND DISCUSSION

Reduction of A-homo-4a-cholesten-3-one (1) [6] with lithium aluminium hydride led to a 1 : 1 mixture of A-homo-4a-cholesten-3α- and -3β-ol (2). Attempted separation into its components by preparative t.l.c. was unsuccessful and the mixture was used as the substrate in the initial experiment. Irradiation of the mixture (2) in benzene containing mercury(II) oxide and iodine (each 3 mol. equiv.) with a 100-W high-pressure mercury arc for 2 h under an atmosphere of nitrogen gave a mixture of products from which a major crystalline product (3) (40%) and two minor amorphous products (4) and (5) were isolated by preparative t.l.c. (Scheme 1).

The molecular formula of the iodine-containing product (3) was confirmed to be $C_{28}H_{47}IO$ by means of mass

spectrometry (m/e 399, $M^+ - I$, 100%) and by the elemental analysis. The i.r. spectrum showed no bands due to hydroxy and carbonyl groups. The n.m.r. spectrum showed a one-proton doublet at τ 5.68 (J 6.0 Hz) and a

(1)

(2)

hν | HgO–I₂

(3) R = I   (4)   (5)
(6) R = H

SCHEME 1
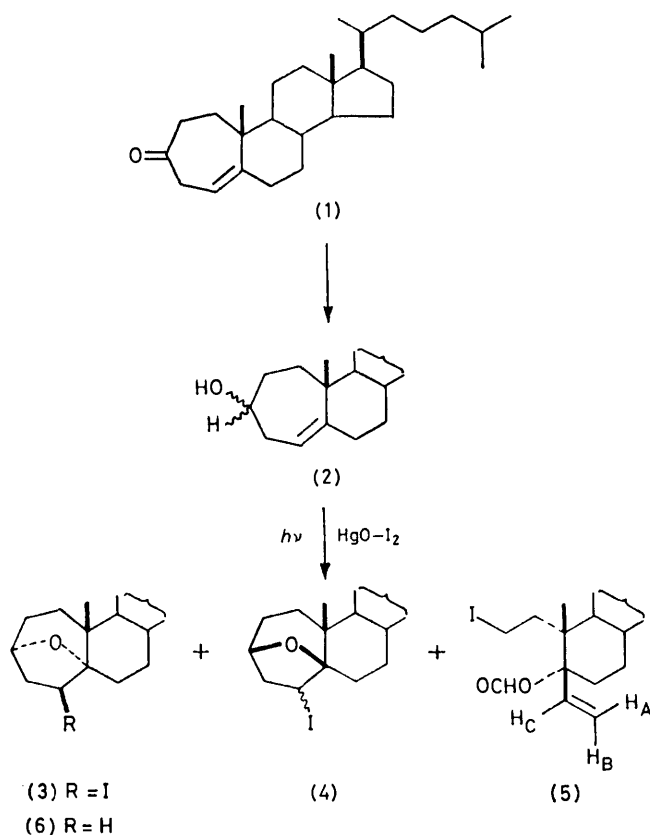
one-proton double doublet at τ 6.31 (J 8.1 and 11.4 Hz). These signals were ascribable to those arising from a hydrogen attached to a carbon carrying an oxygen and a hydrogen attached to a carbon carrying an iodine atom. A double-resonance study showed that the double

doublet at τ 6.31 collapsed to a doublet with J 11.4 Hz by irradiation at τ 7.8, and the doublet at τ 5.68 collapsed to a broad singlet by irradiation at τ 7.3. The ^{13}C n.m.r. spectrum showed three signals at δ 84.19, 75.74, and 56.24, which were assignable (with the aid of off-resonance decoupling) to a quaternary carbon carrying one oxygen (C-5), a carbon carrying one oxygen and one hydrogen (C-3), and a carbon carrying an iodine and one hydrogen (C-4a). Apart from the stereochemistry (see below), these spectral results were consistent with 3,5-epoxy-4a-iodo-A-homocholestane, formed by an intramolecular addition of the 3-oxyl radical. Hydrogenolysis of compound (3) with Raney nickel gave an iodine-free compound (6). Its mass spectrum and the elemental analysis were in accord with the molecular formula $C_{28}H_{48}O$. In its n.m.r. spectrum, a signal arising from a hydrogen attached to the carbon carrying an iodine vanished and only a diffused doublet at τ 5.63, assignable to a signal due to a hydrogen attached to the carbon carrying an oxygen, was present in the downfield region.

Four isomeric structures (A), (B), (C), and (D) with the different orientations of the 3,5-epoxy group and the


(A)   (B)

(C)   (D)

R = H or Me
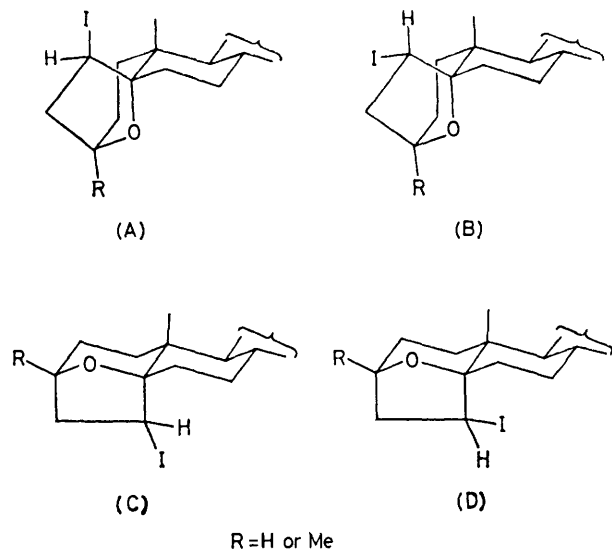
iodine atom are possible for compound (3). A comparison of the n.m.r. spectra of compound (3) and the iodine-free compound (6) showed that the signal arising from the 19-H of (3) appeared at an appreciably lower field (τ 8.65) than that of (6) (τ 9.08). The shift of the signal due to the 19-H of (3) to lower field is attributable to deshielding by the iodine atom, which should be in a *quasi*-1,3-diaxial relationship with the 19-H. Thus the structure 3α,5-epoxy-4aβ-iodo-A-homo-5β-cholestane (A), is the only structure consistent with this n.m.r. spectrum.

Of the two other amorphous products, compound (4), obtained in 7% yield, was shown to be isomeric with A-homo-5β-cholestane (3) by the mass spectrum and the elemental analysis. Its n.m.r. spectrum again showed a one-proton doublet at τ 5.68 (J 7.2 Hz) assigned to a hydrogen attached to a carbon carrying an ether-type oxygen and a one-proton double doublet at τ 6.19 (J 6.9

and 12.0 Hz) ascribable to a hydrogen attached to a carbon carrying an iodine atom. The structure 3α,5-epoxy-4aα-iodo-A-homo-5β-cholestane (B), isomeric with (3) at C-4a, was excluded since the chemical shift of 19-H (τ 8.86) differed considerably from that of the iodine-free compound (6); if it had the structure (B), the chemical shifts of 19-H in the compounds (4) and (6) should be very similar. The chemical shift of the 19-H of (4) was, however, found to be very similar to that of 3β,5-epoxy-3α-methyl-4aα-iodo-A-homo-5α-cholestane (9) obtained from the hypoiodite reaction of 3α-methyl-A-homocholest-4a-en-3β-ol (see below). On the basis of these spectral results, the 3β,5-epoxy-4aα-iodo-A-homo-5α-cholestane structure (C) was assigned to the product (4), formed by intramolecular addition of a 3β-oxyl radical generated from A-homo-4a-cholesten-3β-ol.

The molecular formula of another minor product (5) containing iodine (3% yield) was shown to be $C_{28}H_{47}O_2I$ by the mass spectrum and the elemental analysis. Its n.m.r. spectrum showed a series of signals assignable to a vinyl group and a one-proton singlet at τ 1.88 assignable to a OCHO group. Its i.r. spectrum also showed two intense bands at 1 730 and 1 156 cm^{-1} arising from a formate group. The generation of formates *via* β-cleavage of oxyl radicals in the hypoiodite reactions of cholesterol and the related 5-cholesten-3-ols has already been discussed in the previous papers.[2-4] The formate (5) was generated by a path similar to the one from other 5-cholesten-3-ols. The structure and genesis are shown in Scheme 2.
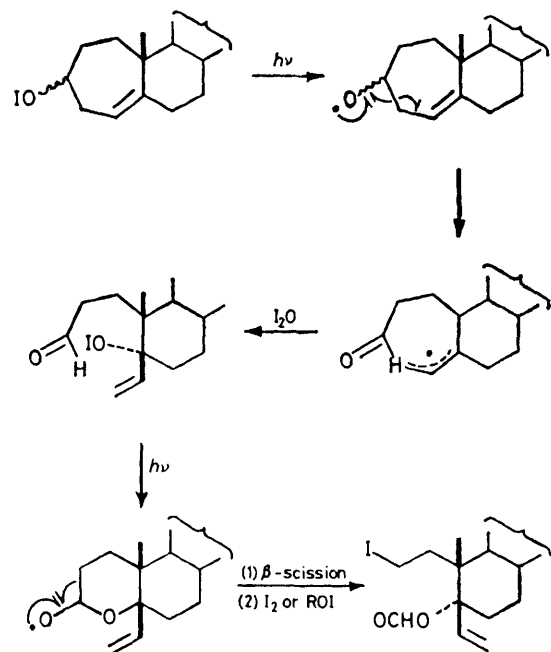
Scheme 2

In order to assess the effect of an alkyl group in the vicinity of an oxyl radical, 3α-methyl-A-homo-4a-cholesten-3β-ol (7) and its 3-epimer (8) were newly synthesized and the hypoiodite reaction of these com-
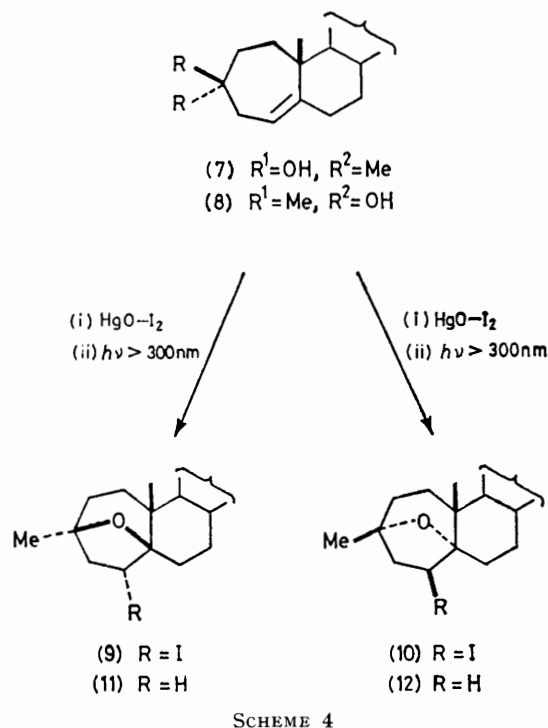
pounds, under similar conditions to those used for compound (2), was attempted. 3α- and 3β-Methyl-A-homo-4a-cholesten-3-ols (7) and (8) were prepared by the reaction of the ketone (1) with methyl-lithium, (Scheme 3). The mixture of the alcohols (7) and (8) formed was separated by means of column chromatography and preparative t.l.c. The yields of the two alcohols (7) and

(1)

↓ MeLi

(7)   +   (8)

Scheme 3
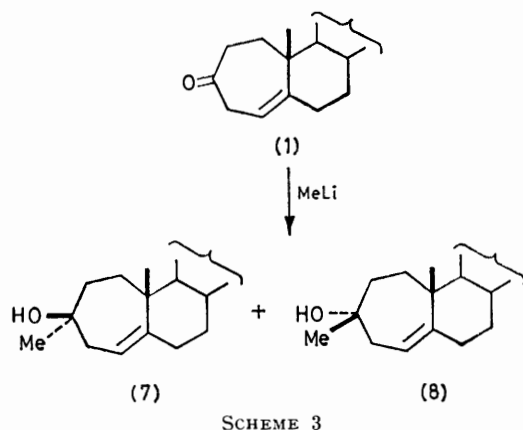
(8) were 44% and 32%. It was not possible to deduce the configurations at C-3 of the alcohols (7) and (8) by spectroscopy, and the alcohol obtained in a greater yield was assigned as the 3β-alcohol (7) solely on considerations of the reaction stereochemistry.

Irradiation of the 3β-alcohol (7) in benzene containing iodine and mercury(II) oxide under conditions similar to the case of alcohol (2) for 8 h gave a product, from which a major compound (9) was obtained by preparative t.l.c. in 48% yield (Scheme 4). Unidentified minor products

derived from it showed only a small upfield shift of the signal due to 19-H in going from compound (9) to compound (11). This result proved that the iodine atom and

(7) R¹=OH, R²=Me
(8) R¹=Me, R²=OH

(i) HgO–I₂
(ii) hν > 300nm

(i) HgO–I₂
(ii) hν > 300nm

(9) R = I
(11) R = H

(10) R = I
(12) R = H

Scheme 4

the 19-H in compound (9) were not in a 1,3-diaxial relationship, and the result was consistent with either of the two structures (C, R = Me) and (D, R = Me), formed by an intramolecular addition of the corresponding 3β-oxyl
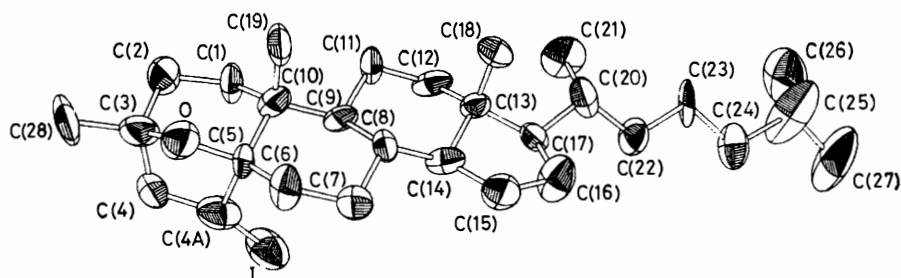
Perspective view of the 3β,5-epoxy-3α-methyl-4aα-iodo-A-homo-5α-cholestane molecule (9)

were also formed in this reaction. Compound (9) had the molecular formula $C_{29}H_{49}IO$ by means of mass spectrometry (m/e 540, M^+, 2.5%) and by elemental analysis. Its n.m.r. spectrum showed a one-proton double doublet at τ 6.14 (J 7.5 and 10.8 Hz) assignable to a hydrogen attached to a carbon bearing an iodine atom. This result, together with the i.r. and the mass spectra, was in agreement with 3β,5-epoxy-3α-methyl-4a-iodo-A-homo-5α-cholestane formed by intramolecular addition of the 3β-oxyl radical. Treatment of this A-homocholestane (9) with Raney nickel gave an iodine-free compound (11). A comparison of the n.m.r. spectra of product (9) and the iodine-free compound (11)

radical. N.m.r. spectroscopy was unable to confirm the orientation of the iodine on C-4a although it was almost certainly α-oriented on the basis of *trans* addition to the double bond. The X-ray crystallographic analysis was undertaken to confirm this stereochemistry.

The molecular framework of compound (9) is shown in the Figure. The atomic parameters, bond distances and angles, and the torsion angles are given in Tables 1—3. The seven-membered ring A has a boat conformation and rings B and C take somewhat distorted chair conformations. Since the iodine atom occupies the α-position of C(4a), which is situated in an axial α-position of ring B, it approaches C(9)-H very closely; the observed I ⋯

TABLE 1

Fractional atomic co-ordinates (standard deviations in parentheses)

Atom	x	y	z
C(1)	0.419(1)	−0.042 2(7)	0.892(1)
C(2)	0.407(1)	−0.066 4(7)	1.017(1)
C(3)	0.508(1)	−0.052 0(8)	1.089(1)
C(4)	0.618(1)	−0.077 7(7)	1.030(1)
C(4a)	0.659(1)	−0.020 0(7)	0.955(1)
C(5)	0.563(1)	0.033 3(6)	0.971(1)
C(6)	0.607(1)	0.104 0(7)	0.978(1)
C(7)	0.637(1)	0.129 1(7)	0.857(1)
C(8)	0.538(1)	0.123 4(6)	0.773(1)
C(9)	0.487(1)	0.053 8(7)	0.769(1)
C(10)	0.456(1)	0.029 7(6)	0.893(1)
C(11)	0.387(1)	0.050 1(7)	0.685(1)
C(12)	0.420(1)	0.074 6(7)	0.563(1)
C(13)	0.465(1)	0.142 3(6)	0.568(1)
C(14)	0.567(1)	0.142 3(7)	0.651(1)
C(15)	0.622(1)	0.208 2(8)	0.627(1)
C(16)	0.601(1)	0.222 2(7)	0.499(1)
C(17)	0.525(1)	0.168 9(6)	0.453(1)
C(18)	0.369(1)	0.189 7(7)	0.602(1)
C(19)	0.358(1)	0.073 1(9)	0.945(1)
C(20)	0.449(1)	0.192 6(7)	0.351(1)
C(21)	0.367(1)	0.140 9(8)	0.304(2)
C(22)	0.525(1)	0.217 1(7)	0.252(1)
C(23)	0.461(1)	0.253 2(7)	0.160(1)
C(24)	0.546(1)	0.284 9(7)	0.081(1)
C(25)	0.480(2)	0.329 2(11)	−0.010(1)
C(26)	0.407(2)	0.299 6(11)	−0.072(2)
C(27)	0.575(2)	0.356 9(13)	−0.089(2)
C(28)	0.488(1)	−0.074 1(8)	1.217(1)
O	0.524 5(8)	0.017 5(5)	1.088 5(8)
I	0.736 8(1)	−0.047 48(6)	0.802 8(1)

TABLE 2

Bond lengths (Å) and angles (°) (standard deviations are referred to the last digits)

C(1)–C(2)	1.54(2)	C(2)–C(1)–C(10)	109(1)
C(1)–C(10)	1.54(2)	C(1)–C(2)–C(3)	113(1)
C(2)–C(3)	1.49(2)	C(2)–C(3)–C(4)	110(1)
C(3)–C(4)	1.56(2)	C(2)–C(3)–C(28)	111(1)
C(3)–C(28)	1.57(2)	C(2)–C(3)–O	108(1)
C(3)–O	1.44(2)	C(4)–C(3)–C(28)	116(1)
C(4)–C(4a)	1.55(2)	C(4)–C(3)–O	103(1)
C(4a)–C(5)	1.58(2)	C(28)–C(3)–O	108(1)
C(4a)–I	2.07(2)	C(3)–C(4)–C(4a)	104(1)
C(5)–C(6)	1.54(2)	C(4)–C(4a)–C(5)	104(1)
C(5)–C(10)	1.55(2)	C(4)–C(4a)–I	114(1)
C(5)–O	1.48(2)	C(5)–C(4a)–I	127(1)
C(6)–C(7)	1.54(2)	C(4a)–C(5)–C(6)	115(1)
C(7)–C(8)	1.53(2)	C(4a)–C(5)–C(10)	118(1)
C(8)–C(9)	1.55(2)	C(4a)–C(5)–O	100(1)
C(8)–C(14)	1.51(2)	C(6)–C(5)–C(10)	110(1)
C(9)–C(10)	1.56(2)	C(6)–C(5)–O	105(1)
C(9)–C(11)	1.53(2)	C(10)–C(5)–O	106(1)
C(10)–C(19)	1.58(2)	C(5)–C(6)–C(7)	110(1)
C(11)–C(12)	1.55(2)	C(6)–C(7)–C(8)	113(1)
C(12)–C(13)	1.49(2)	C(7)–C(8)–C(9)	113(1)
C(13)–C(14)	1.54(2)	C(7)–C(8)–C(14)	114(1)
C(13)–C(17)	1.61(2)	C(9)–C(8)–C(14)	107(1)
C(13)–C(18)	1.54(2)	C(8)–C(9)–C(10)	111(1)
C(14)–C(15)	1.53(2)	C(8)–C(9)–C(11)	111(1)
C(15)–C(16)	1.53(2)	C(10)–C(9)–C(11)	114(1)
C(16)–C(17)	1.51(2)	C(1)–C(10)–C(5)	106(1)
C(17)–C(20)	1.56(2)	C(1)–C(10)–C(9)	111(1)
C(20)–C(21)	1.53(2)	C(1)–C(10)–C(19)	110(1)
C(20)–C(22)	1.55(2)	C(5)–C(10)–C(9)	110(1)
C(22)–C(23)	1.50(2)	C(5)–C(10)–C(19)	110(1)
C(23)–C(24)	1.51(2)	C(9)–C(10)–C(19)	110(1)
C(24)–C(25)	1.60(3)	C(9)–C(11)–C(12)	112(1)
C(25)–C(26)	1.28(3)	C(11)–C(12)–C(13)	111(1)
C(25)–C(27)	1.55(3)	C(12)–C(13)–C(14)	107(1)
		C(12)–C(13)–C(17)	116(1)
		C(12)–C(13)–C(18)	110(1)
		C(14)–C(13)–C(17)	100(1)
		C(14)–C(13)–C(18)	114(1)
		C(17)–C(13)–C(18)	109(1)
		C(8)–C(14)–C(13)	114(1)
		C(8)–C(14)–C(15)	120(1)
		C(13)–C(14)–C(15)	102(1)
		C(14)–C(15)–C(16)	106(1)
		C(15)–C(16)–C(17)	108(1)
		C(13)–C(17)–C(16)	102(1)
		C(13)–C(17)–C(20)	119(1)
		C(16)–C(17)–C(20)	113(1)
		C(17)–C(20)–C(21)	115(1)
		C(17)–C(20)–C(22)	110(1)
		C(21)–C(20)–C(22)	109(1)
		C(20)–C(22)–C(23)	113(1)
		C(22)–C(23)–C(24)	108(1)
		C(23)–C(24)–C(25)	110(1)
		C(24)–C(25)–C(26)	115(2)
		C(24)–C(25)–C(27)	105(2)
		C(26)–C(25)–C(27)	109(2)
		C(3)–O–C(5)	105(1)

C(9) distance of 3.62(1) Å is considerably smaller than the sum of the van der Waals radii, 4.15 Å. This strong steric repulsion results in a great enlargement of the I–C(4a)–C(5) and C(4a)–C(5)–C(10) bond angles, their observed values being 127 and 118°, respectively. Ring D adopts a somewhat deformed envelope conformation with an approximate mirror plane through the C(13) atom. The C(25)–C(26) distance of 1.28 Å is very small as compared with the accepted value for C–C single bonds. This may be due to the large thermal motion of the C(25) and C(26) atoms.

Irradiation of the 3α-alcohol (8) in benzene under the conditions comparable to those used for the 3β-alcohol (7) similarly gave a crystalline compound (10) as the major product (Scheme 4). Its n.m.r. spectrum showed a one-proton triplet at τ 9.3 with J 9.3 Hz assignable to a hydrogen attached to the carbon carrying an iodine atom. The 3-methyl-3,5-epoxy-4a-iodo-A-homocholestane structure formed by radical addition was in agreement with these results, together with the mass and i.r. spectra and the elemental analysis. Removal of the iodine atom from the product (10) as in the case of product (9) gave an iodine-free compound (12) which was not identical with the iodine-free compound (11). A comparison of the n.m.r. spectra of product (10) and the iodine-free compound (12) derived from it showed a considerable upfield shift (Δδ 0.50 p.p.m.) of the signal due to 19-H in going from compound (10) to compound (12), proving a *quasi* 1,3-diaxial relationship between 19-H and the iodine atom in compound (10). The structure 3α,5-epoxy-3β-methyl-4aβ-iodo-A-homo-5β-

cholestane (10) was the only one which was consistent with this n.m.r. spectrum.

These experiments thus confirmed that the predominant reaction of the 3-oxyl radicals generated from A-homo-4a-cholesten-3α- and -3β-ols and their 3-methyl derivatives was an intramolecular radical addition to the 5,6-double bond, and not β-cleavage which was found to be the almost exclusive reaction in the hypoiodites of 3-hydroxy-Δ^5-steroids. The observed products from the intramolecular addition were apparently the kinetically controlled ones. In these intramolecular radical additions the 3-oxyl radical should be appropriately located to the 5,6-double bond.

TABLE 3
Torsion angles (°)

Ring A		
C(10)–C(1)–C(2)–C(3)		−50
C(1)–C(2)–C(3)–C(4)		−53
C(2)–C(3)–C(4)–C(4a)		89
C(3)–C(4)–C(4a)–C(5)		−3
C(4)–C(4a)–C(5)–C(10)		−85
C(4a)–C(5)–C(10)–C(1)		45
C(5)–C(10)–C(1)–C(2)		53
Ring B		
C(10)–C(5)–C(6)–C(7)		−59
C(5)–C(6)–C(7)–C(8)		55
C(6)–C(7)–C(8)–C(9)		−52
C(7)–C(8)–C(9)–C(10)		53
C(8)–C(9)–C(10)–C(5)		−56
C(9)–C(10)–C(5)–C(6)		60
Ring C		
C(14)–C(8)–C(9)–C(11)		−54
C(8)–C(9)–C(11)–C(12)		54
C(9)–C(11)–C(12)–C(13)		−57
C(11)–C(12)–C(13)–C(14)		57
C(12)–C(13)–C(14)–C(8)		−62
C(13)–C(14)–C(8)–C(9)		60
Ring D		
C(17)–C(13)–C(14)–C(15)		45
C(13)–C(14)–C(15)–C(16)		−32
C(14)–C(15)–C(16)–C(17)		6
C(15)–C(16)–C(17)–C(13)		22
C(16)–C(17)–C(13)–C(14)		−41
Side-chain		
C(13)–C(17)–C(20)–C(22)		179
C(17)–C(20)–C(22)–C(23)		−168
C(20)–C(22)–C(23)–C(24)		170
C(22)–C(23)–C(24)–C(25)		−175
C(23)–C(24)–C(25)–C(26)		−58

A sesquiterpene, widdrol (13), has a structural unit corresponding to the A- and B-rings of 3α-methyl-A-homo-4a-cholesten-3β-ol, except that it has *gem*-dimethyl groups on the carbon corresponding to C(6) of the steroids. It has recently been shown that irradiation of the hypoiodite of widdrol (14) resulted in exclusive β-scission of the corresponding 3β-oxyl radical (15) and gave a cyclic iodine-containing ether (16),[7] but no products from intramolecular addition were formed. The result is thus in sharp contrast with the present result.

(13) R = H
(14) R = I
(15)
(16)
(17)
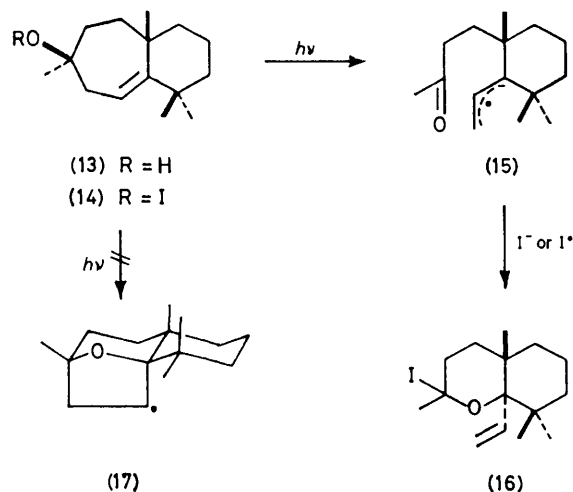
SCHEME 5

The result for widdrol hypoiodite shows the importance of steric effects for the pathway from an oxyl radical incorporated in the A-homo-4a-cholestene framework. Thus the rigid intermediate radical (17) formed from intramolecular addition to the double bond of the oxyl radical generated from widdrol (or the preceding transition state) involves a 1,3-diaxial interaction between the angular methyl and one of the *gem*-dimethyl groups. The intramolecular addition of the oxyl radical from widdrol should thus be much slower and result in the observed β-scission.

These results thus show that the intramolecular addition of oxyl radicals is a faster process than β-scission even in oxyl radicals generated from the hypoiodites of homoallyl alcohols (which are very susceptible to β-scission) provided the oxyl radical is appropriately located to the double bond, and demonstrate that it may provide a useful synthetic route to the 1-oxabicyclo-[1.2.3]heptane system.

It has been reported[8] that oxyl radicals generated from the photolysis of the nitrites of open-chain γδ-unsaturated alcohols underwent intramolecular addition to give tetrahydrofuran derivatives, and that some bridged oxabicyclic compounds can be synthesized by the photolysis of cyclic unsaturated alcohol nitrites.[9]

EXPERIMENTAL

For instruments used and general procedure see ref. 2.
A-*Homo*-4a-*cholesten*-3-*one* (1).—This ketone was prepared by a procedure described by Johnson *et al.*,[6] m.p. 91.5—94.0 °C (lit.,[6] 90.0—94.0 °C).

Reduction of A-*Homo*-4a-*cholesten*-3-*one with Lithium Aluminium Hydride*.—The ketone (1) (1.686 g) and lithium aluminium hydride (450 mg) in dry diethyl ether (60 ml) were stirred for 30 min. After the addition of further lithium aluminium hydride (20 mg), the solution was stirred for another 30 min. The excess of lithium aluminium hydride was decomposed by the addition of ethyl acetate and ice, and the solution was extracted with diethyl ether. The solution was washed with dilute hydrochloric acid and water, and dried over sodium sulphate. The residue (1.561 g) was recrystallized from methanol to yield a mixture of isomeric 3-ols (1.305 g) in two crops, m.p. 119.5—121.0 °C (Found: C, 83.25; H, 12.3. Calc. for $C_{28}H_{48}O$: C, 83.51; H, 12.52%); $v_{max.}$ 3 320 cm^{-1} (OH); τ 9.35 (3 H, s, 18-Me), 9.02 (3 H, s, 19-Me of 3α-ol), 8.99 (3 H, s, 19-Me of 3β-ol), 6.0 (1 H, m, 3-H), and 4.80 (1 H, t, *J* 10 Hz, 4a-H); *m/e* 400 (M^+, 61.8%), 385 ($M^+ -$ Me, 12.9), 382 ($M^+ - H_2O$, 52.0), 367 ($M^+ - H_2O -$ Me, 14.3), 147 (59.8), 95 (91.2), 81 (97.9), 55 (97.6), and 43 (100%).

Irradiation of A-*Homo*-4a-*cholesten*-3-*ols in the Presence of Mercury*(II) *Oxide and Iodine*.—A mixture (602 mg) of A-homo-4a-cholesten-3-ols in benzene (75 ml) containing mercury(II) oxide (1.02 g) and iodine (570 mg) was irradiated for 2 h with a 100-W high-pressure mercury arc under an atmosphere of nitrogen at room temperature. The solution was washed with water and then with aqueous sodium thiosulphate, and the aqueous washings extracted with benzene. The combined organic fractions were dried over anhydrous sodium sulphate. After evaporation of the solvent, the residue (771 mg) was subjected to preparative t.l.c. (Wako gel B-5) eluting with benzene–hexane (1 : 3).

Five fractions (A—E) were obtained. The most mobile fraction A (30 mg) and the least mobile fraction E (175 mg) were intractable products. Fraction B (399 mg) was recrystallized from acetone to yield 3α,5-*epoxy*-4aβ-*iodo*-A-*homo*-5β-*cholestane* (3) (317 mg), m.p. 105.5—106.0 °C, in two crops (Found: C, 63.9; H, 9.05; I, 24.7. $C_{28}H_{47}IO$ requires C, 63.86; H, 9.00; I, 24.11%); $[\alpha]_D^{19.5}$ 52.0 (c 1.2, $CHCl_3$); $\nu_{max.}$ 1 004, 809, and 724 cm^{-1}, no hydroxy or carbonyl bands; τ 9.35 (3 H, s, 18-Me), 8.65 (3 H, s, 19-Me), 6.31 (1 H, dd, J 8.1 and 11.4 Hz, 4aα-H), and 5.68 (1 H, br d, J 6.0, 3β-H); m/e 399 (M^+ — I, 100%), 381 (6.4), and 95 (47.3).

The fractions C (87 mg) and D (72 mg) were combined and subjected to preparative t.l.c. eluting with hexane–ethyl acetate (11 : 1) to afford three fractions. The most mobile amorphous fraction (26 mg) was the *formate* (5), m/e 542 (M^+) (Found: C, 61.6; H, 8.4. $C_{28}H_{47}IO_2$ requires C, 61.98; H, 8.73%); $\nu_{max.}$ (neat) 1 730 (OCHO), 1 437, 1 372, 1 156, 902, and 732 cm^{-1}; τ 9.38 (3 H, s, 18-Me), 9.23 (3 H, s, 19-Me), 6.6 (2 H, m, 2-H), 4.84 (1 H, d, J 18.0 Hz, H_A of vinyl group), 4.59 (1 H, d, J 11.4 Hz, H_B of vinyl group), 3.98 (1 H, dd, J 18.0 and 11.4 Hz, H_C of vinyl group), and 1.88 (1 H, s, formyloxy). The second mobile fraction (76 mg) was again purified by column chromatography (Wako gel C-200, 2 g). Elution with hexane–benzene (1 : 1) gave the isomeric cyclic ether (4) (58 mg) as an amorphous powder (Found: C, 63.7; H, 9.1; I, 24.5. $C_{28}H_{47}IO$ requires C, 63.86; H, 9.00; I, 24.11%); $\nu_{max.}$ 1 221, 1 143, 1 036, and 742 cm^{-1}; τ 9.34 (3 H, s, 18-H), 8.86 (3 H, s, 19-H), 6.19 (1 H, dd, J 6.9 and 12.0 Hz, 4a-H), and 5.68 (1 H, d, J 7.2 Hz, 3β-H); m/e 399 (M^+ — I, 100%).

Synthesis of 3α-*Methyl*-A-*homo*-4a-*cholesten*-3β-*ol* (7) *and* 3β-*Methyl*-A-*homo*-4a-*cholesten*-3α-*ol* (8).—To the ketone (1) (2.172 g) in dry diethyl ether (50 ml) was added methyl-lithium [from methyl iodide (17 ml) and lithium metal (4.1 g) in dry diethyl ether (200 ml)] at 0 °C during 5 min, and the solution was stirred for 4.5 h. To the reaction mixture were added ammonium chloride and then ice, and the solution was washed successively with 2N hydrochloric acid, saturated sodium thiosulphate, sodium chloride solution, and water, and dried over sodium sulphate. After the evaporation of the solvent, the residue was subjected to column chromatography (Wako gel C-200, 100—200 mesh, 55 g). Elution with hexane, hexane–benzene with an increasing amount of benzene, and then benzene gave four fractions. The first fraction (426 mg) was subjected to preparative t.l.c. with hexane–diethyl ether–ethyl acetate–acetone (50 : 1 : 1 : 1). Double development of the plates gave four fractions. The most mobile fraction (353 mg) was compound (8). The next mobile fraction (826 mg) was a mixture of 3α- and 3β-ols. This mixture was again subjected to preparative t.l.c. with hexane–diethyl ether–ethyl acetate–acetone (50 : 1 : 1 : 1). The plates were developed three times to give a more mobile 3β-ol (205 mg) and a less mobile 3α-ol (380 mg). The third mobile fraction (644 mg) was almost pure 3β-ol. The least mobile fraction (136 mg) was 3β-ol. Yields of the 3α-ol and the 3β-ol were 44% and 32%. The 3β-ol (7) was amorphous (Found: C, 83.9; H, 12.55. $C_{28}H_{48}O$ requires C, 83.58; H, 12.58%); $\nu_{max.}$ 3 373 (OH), 1 129, 961, 861, 880, and 852 cm^{-1}; τ 9.32 (3 H, s, 18-Me), 8.98 (3 H, s, 19-Me), 8.77 (3 H, s, 3α-Me), and 4.80 (1 H, t, J 6.0); m/e 414 (M^+, 6.1%), 343 (100), 135 (29.1), 121 (28.4), 109 (52.4), 107 (50.9), 95 (94.2), 81 (64.0), 69 (28.8), 55 (50.4), and 43 (51.9). The 3α-ol (8) was also amorphous (Found: C, 83.55; H, 12.75; $C_{28}H_{48}O$ requires

C, 83.58; H, 12.58%); $\nu_{max.}$ 3 360 (OH), 1 251, 1 111, 1 064, 943, 897, and 863 cm^{-1}; τ 9.32 (3 H, s, 18-Me), 8.94 (3 H, s, 19-Me), 8.76 (3 H, s, 3β-Me), and 4.83 (1 H, dd, J 6.0 and 7.5, 4a-H); m/e 414 (M^+).

Irradiation of 3α-*Methyl*-A-*homo*-4a-*cholesten*-3β-*ol* (7) *in the Presence of Mercury*(II) *Oxide and Iodine.*—The 3β-ol (586 mg) in benzene (63 ml) in the presence of mercury(II) oxide (905 mg) and iodine (534 mg) was irradiated for 8 h under an atmosphere of nitrogen. After the removal of some insoluble material by filtration, the solution was washed with aqueous sodium thiosulphate and then water, and dried over sodium sulphate. After evaporation of the solvent, the residue (713 mg) was subjected to preparative t.l.c. with benzene–hexane (1 : 4) to give four fractions, A (3 mg), B (53 mg), C (398 mg), and D (14 mg) in the order of their mobility. The most mobile fraction was an amorphous seco-steroid. Its n.m.r. spectrum showed signals due to the olefinic protons of a vinyl group. Fraction C (398 mg) was recrystallized from acetone to yield the iodide (9) (354 mg) in two crops, m.p. 128—130 °C, $[\alpha]_D^{18.5}$ —19.6° (c 1.12, $CHCl_3$) (Found: C, 64.15; H, 9.15; I, 23.45. $C_{29}H_{49}IO$ requires C, 64.43; H, 9.13; I, 23.48%); $\nu_{max.}$ 1 100, 1 020, 984, and 877 cm^{-1}; τ 9.34 (3 H, s, 18-Me), 8.86 (3 H, s, 19-Me), 8.68 (3 H, s, 3α-Me), and 6.14 (1 H, dd, J 7.5 and 10.8, 4aβ-H); m/e 540 (M^+, 2.5%), 525 (M^+ — Me, 4.1), 413 (M^+ — I, 100), 395 (27.2), 289 (30.1), 287 (35.5), 109 (61.8), 107 (86.6), 95 (76.4), 81 (91.2), 69 (36.8), 57 (42.8), 55 (41.2), and 43 (41.0). The least mobile fraction (D) was an unidentified gum.

X-*Ray Crystallographic Analysis of* 3β,5-*Epoxy*-3α-*methyl*-4aα-*iodo*-A-*homo*-5α-*cholestane* (9).—Crystal data are as follows. $C_{29}H_{49}IO$, M = 540.61. Orthorhombic, a = 11.746(5), b = 20.547(12), c = 11.635(6) Å, U = 2 808 Å^3, D_c = 1.279 g cm^{-3}, Z = 4, F(000) = 1 136, μ(Mo-K_α) = 11.4 cm^{-1}. Systematic absences: h00 for h odd, 0k0 for k odd, 00l for l odd, space group $P2_12_12_1$.

A single crystal having dimensions ca. 0.3 × 0.3 × 0.2 mm was used for the X-ray measurement. The cell dimensions and reflection intensities were obtained on a Hilger and Watts four-circle diffractometer with Zr-filtered Mo-K_α radiation (λ = 0.710 69 Å). The ω-step-scan technique was applied at intervals of 0.02°; the intensity at each step was measured for 1 s, and the background was measured for 25 s at each end of the scan range. The intensities were corrected for the Lorentz and polarization factors, but not for the absorption or the extinction effect. In the range of 2θ values up to 48°, 1 653 unique structure-factor amplitudes above the 3σ (F) level were selected for the subsequent structure analysis and refinement.

The structure was solved by the Monte Carlo direct method,[10] using the 20 strongest reflections as the starting set. The sixth random phase set which showed a low R_K value of 0.173 led to the correct solution; an E map based on 749 phases afforded 28 of the 31 independent non-hydrogen atoms. The remaining three were located on a difference-Fourier map. The structure thus obtained was refined by the least-squares method with anisotropic temperature factors. After the 30 hydrogen atoms had been located in a second difference-Fourier map, the least-squares refinement was further repeated including these hydrogen atoms and the anomalous dispersion effects of iodine atoms for Mo-K_α radiation. The function minimized was $\Sigma w(|F_o| - |F_c|)^2$ with w = 1/[σ(F)² exp(AX² + BY² + CXY + DX + EY)], where X = $|F_o|$ and Y = sinθ/λ. The A, B, C, D, and E coefficients were determined from the

$|\Delta F|^2$ values. The final R value was 8.1%. The results are given in Tables 1—3.*

All the calculations were performed on a HITAC M-200H computer at the Hokkaido University Computing Center, using our own programs. The atomic scattering factors were taken from international tables.[11]

Irradiation of 3β-Methyl-A-homo-4a-cholesten-3α-ol (8) in the Presence of Mercury(II) Oxide and Iodine.—The 3α-ol (8) (568 mg) in benzene (60 mg) in the presence of mercury(II) oxide (893 mg) and iodine (516 mg) was irradiated for 8 h. The reaction mixture was worked up in a manner similar to the 3β-ol. The product (713 mg) was subjected to preparative t.l.c. eluting with hexane–benzene (4 : 1) to afford two fractions A and B. Fraction A (387 mg) was dissolved in diethyl ether, and addition of methanol to the ethereal solution gave an oily iodide (10) which crystallized, m.p. 56—58 °C, $[\alpha]_D^{19}$ −0.08 (c 1.0, $CHCl_3$) (Found: C, 63.8; H, 9.15; I, 23.25. $C_{29}H_{49}IO$ requires C, 64.43; H, 9.13; I, 23.48%); $\nu_{max.}$ 1 192, 943, 929, and 742 cm^{-1}; τ 9.36 (3 H, s, 18-Me), 8.70 (3 H, s, 19-Me), 8.68 (3 H, s, 3β-Me), and 6.26 (1 H, t, J 9.3, 4aα-H); m/e 540 (M^+, 0.3%), 525 (M^+ − Me, 0.9), 413 (M^+ − I, 100), 395 (8.9), 289 (1.0), 287 (3.2), 109 (39.3), 107 (16.9), 95 (36.6), 81 (38.1), 69 (18.5), 57 (25.5), 55 (23.2), and 43 (24.4). Fraction B (159 mg) was a mixture and no well defined compounds were obtained.

Hydrogenolysis of Iodide (3).—To iodide (3) (52 mg) in dry ethanol (2 ml) and dry diethyl ether (1 ml) was added Raney nickel (prepared from Raney Ni W-4) in ethanol under a hydrogen atmosphere. The solution was stirred for 15 min. After removal of the catalyst by filtration, the solution was evaporated to give gummy residue (41 mg). This was purified by preparative t.l.c. to give the iodine-free compound (6); $\nu_{max.}$ 1 060, 1 011, and 1 039 cm^{-1}; τ 9.34 (3 H, s, 18-Me), 9.08 (3 H, s, 19-Me), and 5.63 (1 H, br d); m/e 574 (M^+, 100%).

* The anisotropic thermal parameters for the non-hydrogen atoms and the co-ordinates and temperature factors for the hydrogen atoms are available in supplementary publication No. SUP 23138 (3 pp.). For details see Notice to Authors No. 7 in *J. Chem. Soc., Perkin Trans. 1*, 1980, Index issue.

Hydrogenolysis of Iodide (9).—To iodide (9) (55 mg) in dry ethanol (2 ml) and dry benzene (1 ml) was added Raney nickel in ethanol (2 ml) under a hydrogen atmosphere, and the solution was stirred overnight. After removal of the catalyst, the solution was evaporated to afford a gum (45 mg); $\nu_{max.}$ 1 124, 1 098, 1 049, 1 030, 981, 932, 912, and 897 cm^{-1}; τ 9.35 (3 H, s, 18-Me), 8.95 (3 H, s, 19-Me), and 8.71 (3 H, s, 3α-Me); m/e 588 (M^+, 100%).

Hydrogenolysis of Iodide (10).—To iodide (10) (50 mg) in dry ethanol (2 ml) and dry benzene (1 ml) was added Raney nickel in ethanol (3 ml) under a hydrogen atmosphere, and the solution was stirred overnight. After removal of the catalyst, the solution was evaporated to give a gum (26 mg); $\nu_{max.}$ 1 125, 1 102, 943, and 930 cm^{-1}; τ 9.35 (3 H, s, 18-Me), 9.20 (3 H, s, 19-Me), and 8.73 (3 H, s, 3β-Me); m/e 588 (M^+, 100%).

REFERENCES

[1] Part 56; H. Suginome, N. Maeda, Y. Takahashi, and N. Miyata, *Bull. Chem. Soc. Jpn.*, 1981, **54**, 846.
[2] H. Suginome, A. Furusaki, K. Kato, N. Maeda. and F. Yonebayashi, *J. Chem. Soc., Perkin Trans. 1*, 1981, 236.
[3] H. Suginome and N. Maeda, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 2621.
[4] H. Suginome and N. Maeda, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 2626.
[5] H. Suginome, K. Kato, and T. Masamune, *Bull. Chem. Soc. Jpn.*, in the press.
[6] W. S. Johnson, N. Neeman, S. P. Birkeland, and N. A. Fedoruk, *J. Am. Chem. Soc.*, 1962, **84**, 989.
[7] H. Takahashi, M. Ito, H. Suginome, and T. Masamune, *Chem. Lett.*, 1979, 901.
[8] R. D. Rieke and N. A. Moore, *J. Org. Chem.*, 1971, **37**, 413; M. P. Bertra and J. M. Surzur, *Bull. Soc. Chim. Fr.*, 1973, 2393.
[9] R. Nouguier and J. M. Surzur, *Bull. Soc. Chim. Fr.*, 1973, 2399.
[10] A. Furusaki, *Acta Crystallogr.*, 1979, **A35**, 220.
[11] ' International Tables for X-Ray Crystallography,' Kynoch Press, Birmingham, 1962, vol. 3.