Synthetic Radical Chemistry. Total Synthesis of (±)-Isoamijiol

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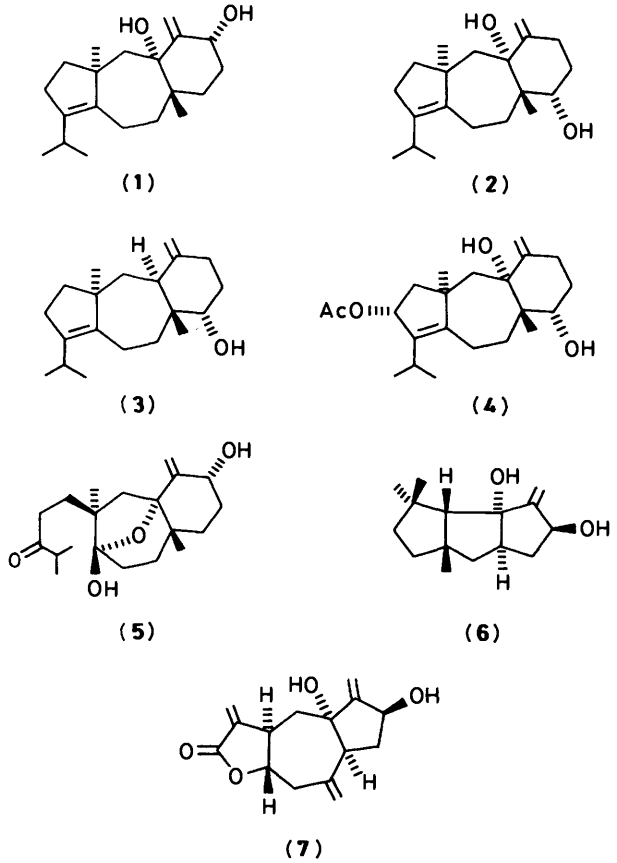
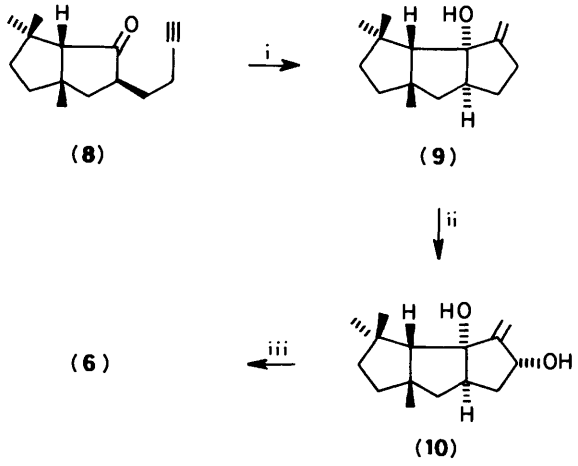
A total synthesis of the dolastane diterpene (±)-isoamijiol (**1**), found in the brown seaweed *Dictyota linearis*, is described. The synthesis, which starts from cyclopentanone, uses just seven carbon-to-carbon bond forming reactions, four of which involve free radical intermediates. The 5,7-ring fused (azulene) portion in (**1**) was elaborated by an intramolecular [2 + 2]-photocycloaddition [*viz.* (**16**)→(**17**)]–intermolecular reductive coupling [*viz.* (**17c**)→(**29**)]–cyclobutane fragmentation [*viz.* (**29**)→(**15**)] sequence, and the 6-ring in compound (**1**) was annulated *via* intramolecular reductive coupling of the terminal acetylenic ketone intermediate (**14**) [to the tricycle (**38**)]. Oxidation of compound (**38**), using catalytic selenium dioxide in the presence of t-butyl hydroperoxide, then produced (±)-isoamijiol which showed spectral data identical with naturally derived material.

Brown seaweeds of the family Dictyotaceae contain a prolific range of antimicrobial and cytotoxic terpenoid secondary metabolites.[1,2] Isoamijiol (**1**), a linear 5,7,6-ring fused member of the dolastane group of diterpenes is the principal secondary metabolite in the brown seaweed *Dictyota linearis*,[3] where it co-occurs with amijiol (**2**), 14-deoxyamijiol (**3**), amijidictyol (**4**), and the seco-dolastane linearol (**5**).[4] A novel feature of isoamijiol (**1**) is the presence of an unusual *bis*-allylic alcohol unit associated with ring C; this feature is also found in the capnellenols, *e.g.*, (**6**), from the coral *Capnella imbricata*,[5] and in arctolides, *e.g.*, (**7**), from *Arctotis grandis*.[6]

In previous work we have developed and applied the principles of intramolecular [2 + 2]-photocycloaddition followed by Grob fragmentation of the resulting cyclobutane adducts, in the synthesis of a range of complex ring-fused natural products, *e.g.*, zizaene, precapnelladiene.[7,8] We have also developed the principles of intramolecular reductive coupling involving acetylenes and allenes in fused ring synthesis,[9] and applied these principles during a total synthesis of (±)-$\Delta^{9(12)}$-capnellene-8β,10α-diol (**6**).[10] In this paper we highlight further scope for the use of free radical reactions, by describing a total synthesis of isoamijiol (**1**) starting from cyclopentanone, which uses only seven carbon-to-carbon bond forming reactions, four of which involve free radical intermediates. Our overall strategy, involved first elaboration of the 5,7-ring fused A/B portion in (**1**) by an intramolecular [2 + 2]-photocycloaddition [*viz.* (**16**)→(**17**)]-intermolecular reductive coupling [*viz.* (**17c**)→(**29**)]-cyclobutane fragmentation [*viz.* (**29**)→(**15**)] sequence, followed by annulation of ring C using intramolecular reductive coupling of the terminal acetylenic ketone intermediate (**14**) [to (**38**)].[11]

Our synthetic investigations amongst the capnellenediol family of marine coral metabolites, *e.g.*, (**6**), had established an expeditious route to the sensitive ene-diol functionality associated with ring C in these structures, based on intramolecular reductive coupling of a terminal acetylenic ketone *viz.* (**8**)→(**9**) followed by regio- and stereo-selective allylic oxidation to the α,α-diol-isomer (**10**) using catalytic selenium dioxide-t-butyl hydroperoxide (Scheme 1). Inversion of the secondary hydroxy group in (**10**) using potassium superoxide–18-crown-6,

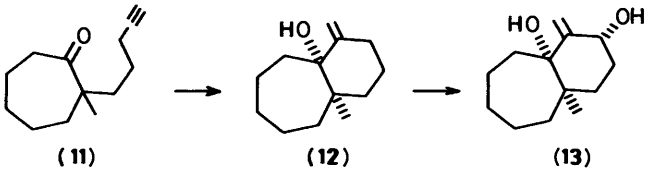




Scheme 1. *Reagents:* i, $C_{10}H_8\bar{N}a$–THF; ii, Bu^tO_2H–SeO_2–CH_2Cl_2; iii, KO_2–18-Crown-6

then completed a synthesis of (±)-$\Delta^{9(12)}$-capnellene-8β,10α-diol (**6**).[10]

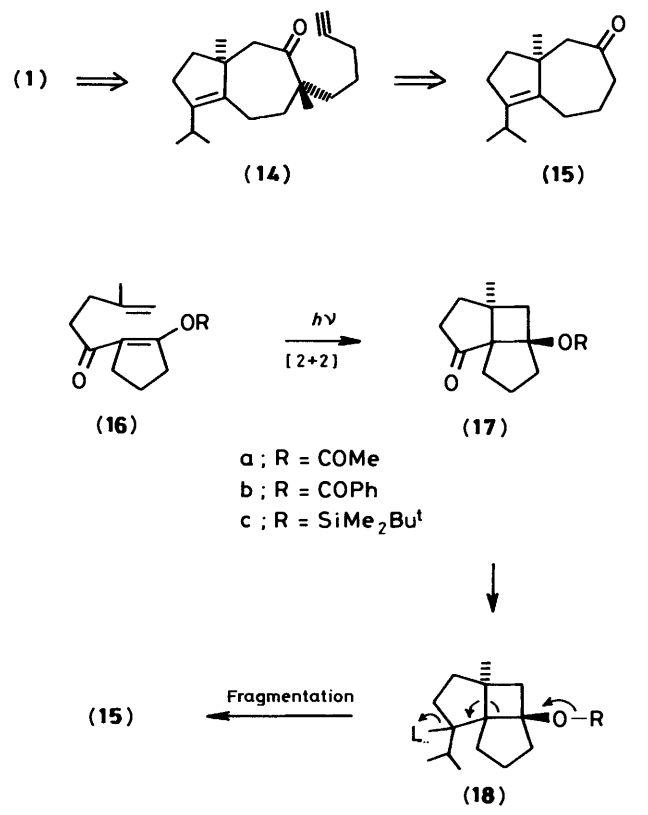
When the general sequence outlined in Scheme 1 was modelled on the 7,6-ring fused system (**13**), present in isoamijiol (**1**) it was found that intramolecular reductive coupling of the conformationally more mobile acetylenic ketone (**11**), using sodium naphthalene radical anion, proceeded equally smoothly to produce the allylic alcohol (**12**), and that oxidation of (**12**) with selenium dioxide–t-butyl hydroperoxide was both clean and stereospecific leading to the crystalline *cis*-ene-α,α-diol (**13**).[9] The *cis*-ring fused geometry assigned to the product (**12**) of cyclisation followed from analysis of ^{13}C n.m.r. shift data and comparison with literature data for *cis*- and *trans*-octahydro-4a*H*-naphthalenol systems.[12]



(**11**) (**12**) (**13**)

With the development of a satisfactory route to the 7,6-ring fused ene-diol system present in isoamijiol (**1**), we turned our attention to the advanced precursor (**14**), which we planned to synthesize from the azulenone (**15**) by sequential regio- and stereo-controlled *gem*-bisalkylation at C-2. We were attracted to the idea of synthesizing the azulenone (**15**) by the intramolecular [2 + 2]-photocycloaddition–cyclobutane fragmentation sequence [(**16**)→(**17**); (**18**)→(**15**)] shown in Scheme 2, and starting from the 3-keto–enol derivative (**16**).[7,8]

Accordingly, we first synthesized the enol derivatives (**16a**), (**16b**), and (**16c**) of the 1,3-dione (**20**) in order to investigate the feasibility of this approach. The 1,3-dione (**20**) was easily obtained from acylation of the enamine (**19**)[13] derived from cyclopentanone with 4-methylpent-4-enoyl chloride,[14] followed by hydrolysis. Acetylation of (**20**) then led to a 2:1 mixture of *exo*-(**21a**) and *endo*-(**16a**) enol acetates, whereas benzoylation and t-butyldimethylsilylation each led to 3:2 mixtures of the corresponding *exo*- and *endo*-enol derivatives. These ratios turned out to have no significance in the subsequent photoreactions, however, since the *exo*- and *endo*-isomers were found to equilibrate on irradiation,[7] and only photoadducts resulting from intramolecular addition with the *endo*-isomers (**16**) were produced. Thus, irradiation of the mixture of enol acetates (**16a**) and (**21a**) in hexane at 25 °C, using Pyrex filtered light from a medium pressure lamp, resulted in regio-selective formation of the crystalline photoadduct (**17a**) in 61% yield; the photoadduct was uncontaminated by its positional isomer (**22**), or by products resulting from photoadditions involving the *exo*-enol acetate (**21a**). In a similar manner the mixture of enol benzoates (**16b**) and (**21b**) led only to (**17b**) (62%) and the enol silyl ethers (**16c**) and (**21c**) produced solely (**17c**) (68%). The structures of the photoadducts (**17a**—**c**) were established, following frag-



Scheme 2.

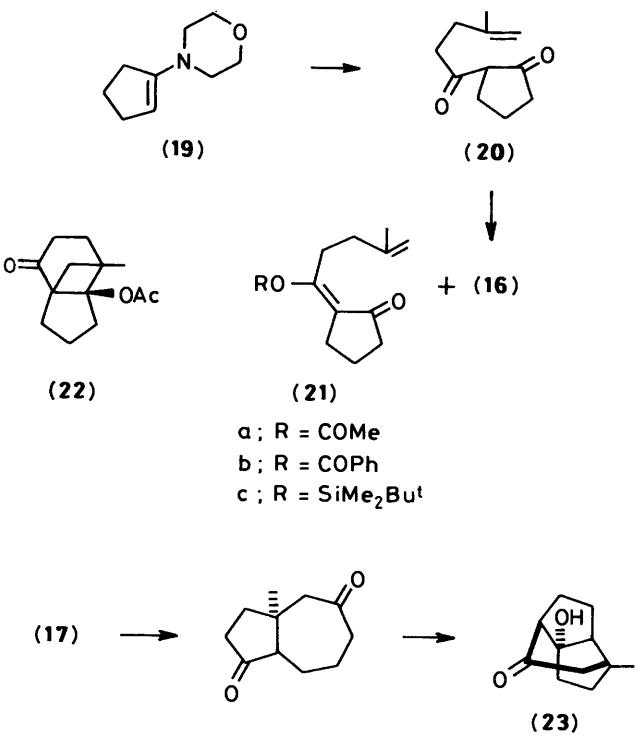


Table 1. Fractional atomic co-ordinates

Atom	*x/a*	*y/b*	*z/c*
C(1)	0.458 6(2)	0.062 2(2)	0.133 0(1)
C(2)	0.254 1(2)	0.098 0(2)	0.144 3(1)
C(3)	0.169 5(2)	0.148 9(2)	0.041 3(1)
C(4)	0.224 0(3)	0.291 5(2)	0.038 5(1)
C(5)	0.318 3(2)	0.319 2(2)	0.144 4(1)
C(6)	0.245 9(2)	0.215 6(2)	0.214 9(1)
C(7)	0.386 7(2)	0.212 6(2)	0.308 4(1)
C(8)	0.564 1(2)	0.281 9(2)	0.272 8(1)
C(9)	0.535 1(2)	0.297 0(2)	0.156 0(1)
C(10)	0.586 5(2)	0.170 1(2)	0.104 5(1)
C(11)	0.651 8(3)	0.406 0(2)	0.114 5(2)
O(12)	0.517 8(2)	−0.046 3(1)	0.145 5(1)
O(13)	0.053 0(2)	0.227 0(1)	0.239 7(1)

Table 2. Bond lengths (Å) with standard deviations in parentheses

C(1)–C(2)	1.506(2)	C(6)–O(13)	1.421(2)
C(1)–C(10)	1.503(2)	C(7)–C(8)	1.538(3)
C(1)–O(12)	1.216(2)	C(7)–H(7a)	0.99(2)
C(2)–C(3)	1.544(2)	C(7)–H(7b)	0.99(2)
C(2)–C(6)	1.539(2)	C(8)–C(9)	1.542(2)
C(2)–H(2)	0.99(2)	C(8)–H(8a)	1.00(2)
C(3)–C(4)	1.539(3)	C(8)–H(8b)	1.02(2)
C(3)–H(3a)	0.99(3)	C(9)–C(10)	1.537(2)
C(3)–H(3b)	0.96(2)	C(9)–C(11)	1.520(2)
C(4)–C(5)	1.537(2)	C(10)–H(10a)	0.97(2)
C(4)–H(4a)	1.03(2)	C(10)–H(10b)	0.99(2)
C(4)–H(4b)	1.07(3)	C(11)–H(11a)	1.03(3)
C(5)–C(6)	1.526(2)	C(11)–H(11b)	1.00(3)
C(5)–C(9)	1.550(2)	C(11)–H(11c)	1.02(3)
C(5)–H(5)	0.99(2)	O(13)–H(13)	0.92(3)
C(6)–C(7)	1.541(2)		
O(13)–O(12)($\frac{1}{2}$ − x, $\frac{1}{2}$ + y, $\frac{1}{2}$ − z)	2.860(2)		
H(13)–O(12)($\frac{1}{2}$ − x, $\frac{1}{2}$ + y, $\frac{1}{2}$ − z)	1.94(3)		

Table 3. Bond angles (°) with standard deviations in parentheses

C(2)–C(1)–C(10)	115.4(1)	C(7)–C(6)–O(13)	114.1(1)
C(2)–C(1)–O(12)	122.9(2)	C(6)–C(7)–C(8)	104.6(1)
C(10)–C(1)–O(12)	121.7(2)	C(6)–C(7)–H(7a)	108(1)
C(1)–C(2)–C(3)	109.4(1)	C(6)–C(7)–H(7b)	114(1)
C(1)–C(2)–C(6)	108.7(1)	C(8)–C(7)–H(7a)	115(1)
C(1)–C(2)–H(2)	111(1)	C(8)–C(7)–H(7b)	113(1)
C(3)–C(2)–C(6)	103.1(1)	H(7a)–C(7)–H(7b)	103(2)
C(3)–C(2)–H(2)	111(1)	C(7)–C(8)–C(9)	106.1(1)
C(6)–C(2)–H(2)	114(1)	C(7)–C(8)–H(8a)	110(1)
C(2)–C(3)–C(4)	105.4(1)	C(7)–C(8)–H(8b)	112(1)
C(2)–C(3)–H(3a)	111(1)	C(9)–C(8)–H(8a)	108(1)
C(2)–C(3)–H(3b)	108(1)	C(9)–C(8)–H(8b)	111(1)
C(4)–C(3)–H(3a)	113(1)	H(8a)–C(8)–H(8b)	110(2)
C(4)–C(3)–H(3b)	110(1)	C(5)–C(9)–C(8)	101.3(1)
H(3a)–C(3)–H(3b)	110(2)	C(5)–C(9)–C(10)	109.8(1)
C(3)–C(4)–C(5)	105.0(1)	C(5)–C(9)–C(11)	113.7(1)
C(3)–C(4)–H(4a)	111(1)	C(8)–C(9)–C(10)	108.9(1)
C(3)–C(4)–H(4b)	112(1)	C(8)–C(9)–C(11)	112.5(2)
C(5)–C(4)–H(4a)	113(1)	C(10)–C(9)–C(11)	110.1(2)
C(5)–C(4)–H(4b)	111(1)	C(1)–C(10)–C(9)	112.3(1)
H(4a)–C(4)–H(4b)	105(2)	C(1)–C(10)–H(10a)	107(1)
C(4)–C(5)–C(6)	105.6(1)	C(1)–C(10)–H(10b)	109(1)
C(4)–C(5)–C(9)	116.4(1)	C(9)–C(10)–H(10a)	111(1)
C(4)–C(5)–H(5)	112(1)	C(9)–C(10)–H(10b)	114(1)
C(6)–C(5)–C(9)	101.1(1)	H(10a)–C(10)–H(10b)	103(2)
C(6)–C(5)–H(5)	112(1)	C(9)–C(11)–H(11a)	112(1)
C(9)–C(5)–H(5)	108(1)	C(9)–C(11)–H(11b)	109(2)
C(2)–C(6)–C(5)	100.3(1)	C(9)–C(11)–H(11c)	114(2)
C(2)–C(6)–C(7)	114.8(1)	H(11a)–C(11)–H(11b)	112(2)
C(2)–C(6)–O(13)	105.6(1)	H(11a)–C(11)–H(11c)	107(2)
C(5)–C(6)–C(7)	105.9(1)	H(11b)–C(11)–H(11c)	103(2)
C(5)–C(6)–O(13)	115.6(1)	C(6)–O(13)–H(13)	109(2)
O(13)–H(13)–O(12)($\frac{1}{2}$ − x, $\frac{1}{2}$ + y, $\frac{1}{2}$ − z)	174(3)		

mentation and aldolisation [aq. NaOH for (**17a**) and (**17b**); aq. HF, then aq. NaOH for (**17c**)] of each to the same highly crystalline tricyclic alcohol (**23**) whose constitution was proven by a single crystal *X*-ray analysis (see Tables 1—3 and Figure).

The regioselectivity observed in the intramolecular [2 + 2]-photocycloaddition from compound (**16**) is quite remarkable, and should be compared and contrasted with our related investigation involving the analogue (**24**) containing a *mono-substituted* double bond in the side chain. In this instance, irradiation was found to produce largely the cross-coupled products (**25**).[7,15] It is also interesting to note that the dimethyl

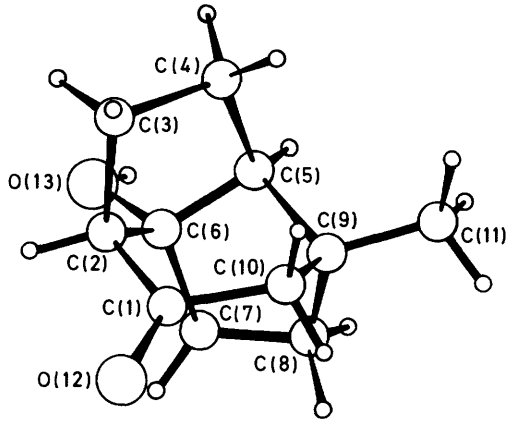
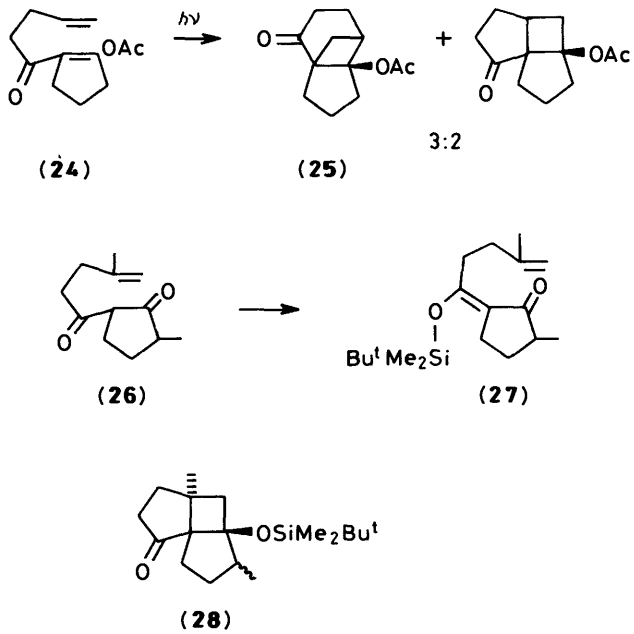


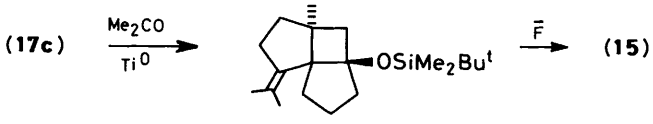
Figure. Crystal structure of compound (**23**)

t-butylsilylation of the 1,3-dione (**26**) [*cf.* (**20**)] led exclusively to the *exo*-enol ether (**27**), which failed completely to isomerise to the *endo*-isomer and, therefore, cyclise to the adduct (**28**) on irradiation. Not for the first time we are witnessing in these examples, *i.e.*, (**16**), (**24**), and (**26**), the remarkable effects that substituents can have in determining the efficacy and directionality of intramolecular photocycloaddition processes.[16]



To complete the synthesis of the azulenone (**15**), it remained only to introduce an isopropyl residue into the cyclopentanone ring in (**17**), prior to Grob fragmentation as indicated in Scheme 2. Since this synthetic operation was likely to lead to problems with the ester groups in compounds (**17a**) and (**17b**), we elected to use the silyl ether adduct (**17c**) for these subsequent steps.[17] Isopropylmagnesium and isopropyl-lithium reagents failed to react with compound (**17c**) under a range of different conditions and solvent combinations;[18] we attributed this to the sterically crowded environment of the carbonyl group in (**17c**) and to the well known ease of enolisation of cyclopentanones.[19,20] Eventually we elaborated the isopropylidene tricycle (**29**) using reductive pinacolic coupling of the ketone (**17c**) with acetone by the McMurry procedure.[21] Thus, addition of a dilute solution of the photoadduct (**17c**) in acetone to a slurry of Ti(0)

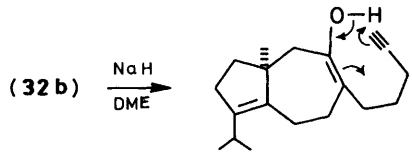
under dimethoxyethane, over 4 h, using a motor syringe, resulted in smooth coupling leading to the alkene (**29**) in 76% yield. Fragmentation of the cyclobutane ring of (**29**) was then smoothly accomplished by brief treatment with aqueous hydrofluoric acid, giving rise to the central azulenone intermediate (**15**). To our knowledge, the Grob fragmentation, (**29**)→(**15**), is the first example of where a C=C double bond and a silicon-oxygen bond have been used as 'pull-push' partners in such a reaction. The synthesis of the azulenone (**15**) from the enamine (**19**), was therefore achieved in only five steps with an overall yield of 20%. This is to be compared with the lengthy non-specific route to (**15**) described previously by Wolf *et al.*[22]



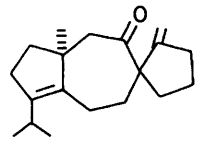
(**29**)

We next turned to the preparation of isoamijiol (**1**) from the advanced precursor (**14**), a process which we planned to achieve *via* sequential pentynylation and methylation of the azulenone (**15**). Deprotonation of compound (**15**) with lithium hexamethyldisilylazide[23] at −15 °C first produced the (kinetic and thermodynamic[24,25]) enolate (**30**), which was then alkylated specifically by the tri-isopropylsilyl protected iodopentyne (**31**)[26] leading to the β-epimer (**32a**) exclusively in 52% yield. The relative stereochemistry in compound (**32a**) followed largely from inspection and comparison of ^{13}C n.m.r. data, and in particular the significant downfield shift (δ 53.7 p.p.m.) observed for the methine (C-6) carbon in the molecule; the latter data indicated that the associated hydrogen atom at C-6 in (**32a**) was approximately perpendicular to the carbonyl group and therefore in a pseudo-axial orientation.[27] Treatment of the pentynylated azulenone (**32a**) with sodium hydride followed by trapping the resulting enolate with methyl iodide next produced (**33**),[25,28] which was smoothly deprotected in the presence of tetrabutylammonium fluoride[29] to the bis-alkylated azulenone (**14**) [44% overall from (**15**)]. The substituted azulenone (**14**) was produced as a 5:1 mixture of α-(**14**) and β-(**35**) epimers; this followed from inspection and quantification of the respective AB quartets centred at δ 2.56 and δ 2.52 for the methylene groups α-to the carbonyl groups in the two isomers. Additionally, these data were compared with corresponding data recorded for the authentic β-epimer (**35**) derived from compound (**15**) by sequential methylation [to (**34**)] and pentynylation.

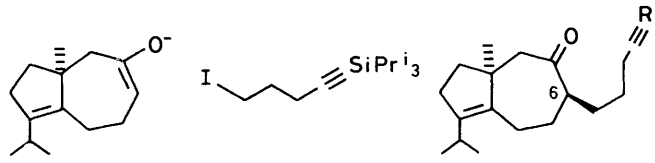
It was interesting to note that the use of the tri-isopropylsilyl protected acetylenic intermediate (**31**) was crucial to the success of the synthesis of (**14**). Attempted deprotonation–methylation of the corresponding *trimethylsilyl* protected acetylenic intermediate (**32b**) instead produced the product (**37**) of an ene reaction, presumably *via* the free acetylenic enol (**36**), exclusively.[30,31]



(**36**)



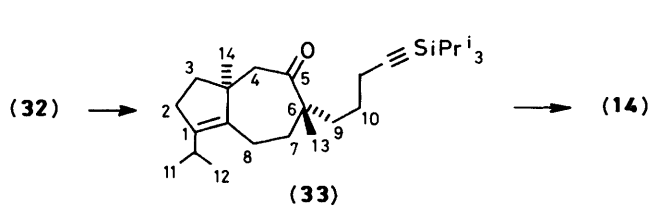
(**37**)



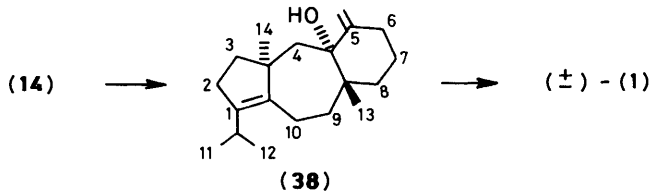
(**30**) (**31**) (**32**)

a; R = $SiPr^i_3$
b; R = $SiMe_3$
c; R = H

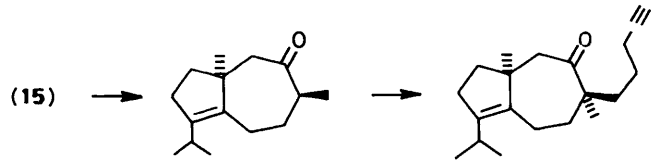
With the correct relative stereochemistry embedded in the acetylenic ketone (**14**) we were in a position to complete our synthesis of isoamijiol (**1**) along parallel lines to those described for the model system (**11**); *i.e.*,→(**12**)→(**13**). Accordingly titration of compound (**14**) with a solution of sodium naphthalene radical anion in tetrahydrofuran, resulted in complete consumption of starting material, and the formation of the *trans*-fused tricyclic alcohol (**38**) in 41% yield. Our original premise, based on inspection of molecular models, that



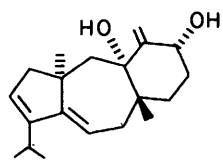
(**33**)



(**38**)



(**34**) (**35**)



(**39**)

steric interactions between the incoming acetylenic side chain and the azulenone ring system would confine ring closure in (**14**) to a *trans*-fused ring junction in (**38**) was fully vindicated by inspection and comparison of the n.m.r. data for compound (**38**) with those of natural isoamijiol itself. Particularly diagnostic were the resonances for the two ring junction methyl groups in compound (**38**), at δ 1.35 and 0.78 p.p.m. which coincided almost exactly with the corresponding resonances *i.e.*, δ 1.34 and 0.77 p.p.m. in isoamijiol (**1**).[3]

The synthesis of (±)-isoamijiol (**1**) was completed by treatment of compound (**28**) with catalytic selenium dioxide in the presence of t-butyl hydroperoxide; as expected, and by comparison with the model system (**13**) this oxidation produced solely the α,α-diol isomer. The synthetic isoamijiol did not separate from naturally derived material in mixed chromatography, and their ^{1}H n.m.r. and m.s. data were superimposable. Disappointingly, a small amount (~12%) of the product (**39**) resulting from over-oxidation of isoamijiol was also produced during the oxidation of compound (**38**),[32] and all attempts to separate this compound from the synthetic isoamijiol proved unsuccessful.

Experimental

For general experimental details see ref. 33.

2-(4-*Methylpent*-4-*enoyl*)*cyclopentanone* (**20**).—A solution of 4-methylpent-4-enoyl chloride (19.39 g)[14] in dry benzene (100 ml) was added dropwise under nitrogen to a rapidly stirred solution of 4-(cyclopent-1-enyl)morpholine (**19**) (22.34 g)[13] and dry triethylamine (20 ml) in dry benzene (130 ml), and the mixture was then stirred under reflux for 12 h. After being cooled to room temperature, the mixture was filtered under suction, and the precipitate of triethylamine hydrochloride was washed with dry ether (3 × 50 ml). The combined filtrates were stirred with dilute hydrochloric acid (2M, 150 ml) for 3 h at room temperature, and the aqueous layer was then separated and extracted with ether (3 × 100 ml). The ether extracts were washed successively with saturated sodium hydrogen carbonate solution (150 ml) and brine (150 ml), then dried, and evaporated to leave a yellow liquid. Distillation gave the 1,3-*dione* (17.61 g, 66.8%) as a pale yellow liquid, b.p. 77—79 °C/0.1 mmHg; $\lambda_{max.}$ 288.25 nm (ε 4 839); $\nu_{max.}$ 1 740, 1 705, 1 650, and 1 605 cm^{-1}; δ_H 4.75 (m, =CH$_2$), 3.81—1.43 (m, 11 H), and 1.73 (m, MeC=); δ_C 212.7, 203.9, 203.8, 179.5, 144.3, 110.6 (t), 110.3 (t), 61.9 (d), 41.3 (t), 38.7 (t), 36.7 (t), 33.2 (t), 33.1 (t), 31.1 (t), 25.8 (t), 25.4 (t), 22.6 (q), 22.4 (q), 20.9 (t), and 20.4 (t) p.p.m.* (Found: *m/z* 180.1161. $C_{11}H_{16}O_2$ requires *M*, 180.1149).

1-[2-(*Acetoxy*)*cyclopent*-1-*enyl*]-4-*methylpent*-4-*en*-1-*one* (**16a**).—A stirred solution of the 1,3-dione (**20**) (2.71 g) in dry pyridine (25 ml) under nitrogen at 0 °C was treated with acetyl chloride (1.1 ml), and the mixture stirred at 0 °C for 3 h. The mixture was poured into ice-cold dilute hydrochloric acid (2M, 250 ml), and then extracted with ether (3 × 100 ml). The combined ether extracts were washed with dilute hydrochloric acid (2M, 100 ml) and then with brine (2 × 150 ml). Evaporation of the dried ether extracts left a pale yellow liquid, which was distilled to give the *enol acetate* (2.64 g, 79%) as a pale yellow liquid, b.p. 107—110 °C/0.6 mmHg. G.l.c. analysis (SE30, 180 °C) showed the presence of *exo*-(**21a**) and *endo*-(**16a**) enol acetate isomers in the ratio 2:1; $\lambda_{max.}$ 250.25 nm (ε 8 099); $\nu_{max.}$ 3 000, 1 775, 1 720, 1 680, and 1 645 cm^{-1}; *exo*-*E*-isomer: δ_H 4.77 (m, =CH$_2$), 3.01 (t, *J* 7 Hz, CH$_2$CO), 2.83—1.65 (m, 8 H), 2.22 (OAc), and 1.77 (MeC=), δ_C 206.5, 167.2, 158.4, 144.6, 125.1, 110.6 (t), 41.4 (t), 34.6 (t), 28.7 (t), 27.8 (t), 22.3 (q), 20.7 (q) and 19.2 (t) p.p.m.; *exo*-*Z*-isomer and *endo*-isomer: δ_H 4.78 (m, =CH$_2$), 2.90—2.75 (m, 4 H), 2.75—1.85 (m, 6 H), 2.27 (OAc), and 1.77 (MeC=); δ_C 203.5, 196.7, 168.3, 167.2, 158.5, 152.7, 145.0, 144.2, 126.2, 122.8, 110.8 (t), 109.8 (t) 40.2 (t), 39.8 (t), 33.6 (t), 33.3 (t), 32.2 (t), 31.6 (t), 29.1 (t), 27.8 (t), 22.7 (q), 22.4 (q), 21.0 (q), 20.9 (q), 19.6 (t), and 19.4 (t) p.p.m.* [Found *m/z* 180.1145 (*M* − OAc). $C_{13}H_{18}O_3$ requires 180.1101].

1-(2-*Benzoyloxycyclopent*-1-*enyl*)-4-*methylpent*-4-*en*-1-*one* (**16b**).—A stirred solution of the 1,3-dione (**20**) (6.27 g) in dry pyridine (25 ml) under nitrogen at 0 °C was treated with benzoyl chloride (5.01 g), and the mixture was then stirred at 0 °C for 4 h. The mixture was poured into ice-cold dilute hydrochloric acid (2M, 250 ml), and then extracted with ether (3 × 100 ml). The combined ether extracts were washed with dilute hydrochloric acid (2M, 100 ml) and brine (2 × 150 ml), dried and evaporated to afford a pale yellow liquid, which was distilled to give the *enol benzoate* (7.76 g, 78.5%) as a pale yellow liquid, b.p. 128—130 °C/0.09 mmHg. G.l.c. analysis (SE30, 230 °C) showed the presence of *exo*- and *endo*-enol benzoate isomers in the ratio 3:2; $\lambda_{max.}$ 236 nm (ε 19 447); $\nu_{max.}$ 1 787, 1 752, 1 710, and 1 665 cm^{-1}; δ_H 8.30—7.93 (m, 2 H, =C*H*), 7.79—7.20 (m, 3 H, =CH), 4.74 and 4.55 (m, =CH$_2$), 3.75—1.53 (m, 10 H), 1.75 and 1.62 (m, MeC=).

1-[2-(*Dimethyl*-*t*-*butylsilyloxy*)*cyclopent*-1-*enyl*]-4-*methylpent*-4-*en*-1-*one* (**16c**).—Dry triethylamine (5.3 ml) was added dropwise to a rapidly stirred solution of the 1,3-dione (**20**) (2.27 g) and t-butyldimethylsilyl chloride (4.20 g) in dry benzene (125 ml) under nitrogen. The mixture was stirred at 60 °C for 12 h, then cooled and quickly filtered under suction. The precipitate of triethylamine hydrochloride was washed with dry hexane (3 × 40 ml), and the combined filtrate was then evaporated. The pale yellow residue was taken up in dry hexane (150 ml), filtered, and re-evaporated to give the silyl ether (3.7 g, 98%) as an oily 3:2 mixture of *exo*- and *endo*-isomers, which was used without further purification; $\nu_{max.}$ 1 702, 1 645, and 1 608 cm^{-1}; δ_H 4.57 (m, =CH$_2$), 2.86—1.51 (m, 10 H), 1.62 (m, MeC=), 0.88 (MeC), and 0.14 (MeSi).

(3aα,4aα,7aS*)-4a-*Acetoxy*-3a-*methyl*-2,3,3a,4,4a,5,6,7-*octahydrocyclobuta*[1,2:1,4]*dicyclopenten*-1-*one* (**17a**).—A solution of the 2:1 mixture of enol acetates (**21a**) and (**16a**) (2.64 g) in dry h.p.l.c. grade hexane (400 ml) was irradiated through Pyrex using a 450 W medium-pressure lamp for 8 h. G.l.c. analysis (SE30, 180 °C) after this time showed almost complete consumption of starting material. The solution was filtered and evaporated to dryness to leave a residue (2.70 g) which was chromatographed on Silica gel G, using ether–light petroleum (b.p. 40—60 °C) (1:1) as eluant, to give the *photoadduct* (1.60 g, 60.6%) which crystallized from hexane as white crystals, m.p. 51—52 °C; $\nu_{max.}$ 1 735 cm^{-1}; δ_H 2.70 (ddd, *J* 18, 12, and 12 Hz, α-C*H*HCO), 2.19 (ddd, *J* 18, 12 and 12 Hz, β-CH*H*CO), 2.19 (2 H), 2.24—1.49 (m, 8 H), 1.94 (OAc), and 1.14 (Me); δ_C 216.0, 169.5, 85.8, 64.4, 45.2 (t), 38.7 (t), 38.2 (t), 37.7, 36.5 (t), 26.3 (t), 25.5 (t), 22.6 (q), and 21.3 (q) p.p.m. (Found: C, 70.0; H, 8.4%; *m/z* 222.1245. $C_{13}H_{18}O_3$ requires C, 70.2; H, 8.2%; *M*, 222.1253).

(3aα,4aα,7aS*)-4a-*Benzoyloxy*-3a-*methyl*-2,3,3a,4,4a,5,6,7-*octahydrocyclobuta*[1,2:1,4]*dicyclopenten*-1-*one* (**17b**).—A solution of the 3:2 mixture of enol benzoates (**21b**) and (**16b**) (2.40 g) in dry h.p.l.c. grade hexane (200 ml) was irradiated through Pyrex using a 450 W medium-pressure lamp for 10 h. G.l.c. analysis (SE30, 230 °C) after this time showed almost complete consumption of starting material. The solution was filtered and evaporated to dryness to leave a residue (2.43 g) which was chromatographed on Silica gel G, using ether–

* Exists as a mixture of *exo*- and *endo*-enol isomers, which interchange within the n.m.r. time scale.

hexane (1:2) as eluant, to give the *photoadduct* (1.48 g, 61.7%) which crystallized from hexane as white crystals, m.p. 87—88 °C; $\nu_{max.}$ 1 715 cm^{-1}; δ_H 7.92 (m, =CH), 7.60—7.34 (m, =CH), 2.76 (ddd, *J* 18, 12, and 12 Hz, α-C*H*HCO), 2.51 (2 H), 2.49 (ddd, *J* 18, 12, and 12 Hz, β-CH*H*CO), 2.32—1.53 (m, 8 H), and 1.18 (Me); δ_C 216.5, 164.8, 133.1 (2 × d), 130.2, 129.5 (d), 128.9 (d), 128.5 (d), 86.0, 64.5, 45.1 (t), 38.8 (t), 38.3 (t), 37.7, 36.5 (t), 26.3 (t), 25.8 (t), and 22.6 (q) p.p.m. (Found: C, 76.0; H, 7.3%; *m/z* 284.1410. $C_{18}H_{20}O_3$ requires C, 76.0, H, 7.1%; *M*, 284.1411).

(3aβ,4aα,7aS*)-3a-*Methyl*-4a-*dimethyl-t-butylsilyloxy*-2,3,3a,4,4a,5,6,7-*octahydrocyclobuta*[1,2:1,4]*dicyclopenten*-1-*one* (**17c**).—A solution of the crude 2:1 mixture of silyl ethers (**21c**) and (**16c**) (3.35 g) in dry h.p.l.c. grade hexane (250 ml) was irradiated through Pyrex using a 450 W medium-pressure lamp for 8 h. G.l.c. analysis (SE30, 220 °C) after this time showed almost complete consumption of starting material. The solution was filtered and evaporated to dryness to leave a residue (3.3 g) which was chromatographed on Silica gel G, using ether–light petroleum (b.p. 40—60 °C) (1:2) as eluant, to give the *photoadduct* (2.28 g, 68.1%) as a colourless oil, b.p. 94—98 °C at 0.1 mmHg, which crystallized on standing to give a waxy solid, m.p. 39—41 °C (ether–pentane 1:2); $\nu_{max.}$ 1 735 cm^{-1}; δ_H 2.73 (ddd, *J* 18, 12, and 12 Hz, α-C*H*HCO), 2.31 (ddd, *J* 18, 12, and 12 Hz, β-CH*H*CO), 2.21 (1 H), 2.16 (1 H), 2.10 (m, 2 H), 2.00—1.44 (m, 6 H), 1.07 (Me), 0.84 (Me_3CSi), 0.06 (MeSi), and 0.03 (MeSi); δ_C 217.3, 83.3, 66.4, 47.9 (t), 41.3 (t), 38.6 (t), 36.9 (t), 36.4, 26.2 (t), 25.7 (3 × q), 25.3 (t), 22.8 (q), 17.8, −2.7 (q), and −3.0 (q) p.p.m. (Found: C, 68.9; H, 10.3%; *m/z* 294.2026. $C_{17}H_{30}O_2Si$ requires C, 69.3; H, 10.3%; *M*, 294.2013).

(1α,3aα)-1,2,3,3a,4,5,6,6a-*Octahydro*-3a-*hydroxy*-1-*methyl*-1,4-*ethanopentalen*-7-*one* (**23**).—(i) Aqueous sodium hydroxide solution (2M, 40 ml) was added to a solution of the photoadduct (**17a**) (56.0 mg) in THF (30 ml), and the mixture stirred at 60 °C for 3 h. After being cooled, the mixture was poured into water (30 ml) and extracted with ether (4 × 25 ml). Evaporation of the dried extracts left the crude product which was purified by chromatography on Silica gel G, using ether–hexane (2:1) as eluant, to give the tricyclic aldol (308.0 mg, 67.8%) as a crystalline solid. Crystallisation from ether-hexane (1:3) gave the *aldol* as hexagonal plates, m.p. 153—155 °C; $\nu_{max.}(CHCl_3)$ 3 600 and 1 703 cm^{-1}; δ_H 3.41 (m, OH), 2.68—1.49 (m, 12 H), and 1.04 (Me); δ_C 211.8, 89.3, 63.8 (d), 57.4 (d), 48.1 (t), 43.6 38.1 (t), 31.8 (t), 28.1 (t), 24.6 (q), and 21.3 (t) p.p.m. (Found: C, 73.4; H, 9.4%; *m/z* 180.1121. $C_{11}H_{16}O_2$ requires C, 73.3; H, 8.95%; *M*, 180.1149).

Similarly, by the above procedure, the photoadduct (**17b**) (176.3 mg) gave the same tricyclic aldol (**23**) (61.1 mg, 54.7%) as a white crystalline solid, m.p. 152—154 °C.

(ii) Aqueous hydrofluoric acid (40%, 4.0 ml) was added in one portion to a stirred solution of the photoadduct (**17c**) (139 mg) in THF (4.0 ml). The mixture was stirred at room temperature for 3 h, aqueous sodium hydroxide (2M, 20 ml) was added, and the mixture was stirred at 60 °C for a further 3 h. On being cooled, the mixture was poured into water (20 ml) and extracted with ether (3 × 20 ml). Evaporation of the dried extracts left the crude aldol which was purified by chromatography on Silica gel G, using ether–hexane (2:1) as eluant to give the tricyclic aldol (83.8 mg, 98.3%) as a white crystalline solid, m.p. 152—154 °C, showing spectral data identical with those described above.

Crystallographic Analysis of (**23**). *Crystal Data.*—$C_{11}H_{16}O_2$, M = 180.25. Monoclinic, a = 7.063(1), b = 10.438(1), c = 13.101(1) Å, β = 92.74(1)°, U = 964.81 Å^3, Z = 4, D_c = 1.24 g cm^{-3}, $F(000)$ = 392, space group $P2_1/n$, Cu-K_α radiation, λ = 1.541 78 Å, μ(Cu-K_α) = 6.76 cm^{-1}.

A crystal of approximate dimensions 0.55 × 0.35 × 0.2 mm^3 was mounted on an Enraf-Nonius CAD4 diffractometer and 25 reflections were used to determine accurate lattice parameters. Intensity data were collected using an ω–2θ scan for 1° ⩽ θ ⩽ 76°. A total of 2 007 independent reflections was measured of which 1 522 had $I > 3\sigma(I)$ and were considered observed and used in the subsequent refinement. The data were corrected for Lorentz and polarisation factors but no absorption corrections were made. Crystallographic calculations were performed using the CRYSTALS system of programs.[34] The structure was solved by direct methods using the MULTAN program.[35] Least squares refinement including anisotropic thermal parameters for non-hydrogen atoms and isotropic refinement of hydrogen atoms located in a difference Fourier synthesis terminated at R 0.0508 (R_w 0.0582). A final difference map showed no features in excess of 0.2 eÅ^{-3}.

The crystal structure is shown in the figure. The cyclohexanone ring adopts the expected chair conformation while the cyclopentane rings are in different conformations. Ring 2,3,4,5,6 is in the envelope conformation with C(6) the flap, while ring 5,6,7,8,9 adopts the half chair shape with the pseudo 2-fold axis midway along the C(5)–C(9) bond. The remaining geometric data are unexceptional. Final atomic coordinates, bond lengths and bond angles are collected in the Tables. Thermal parameters and hydrogen atom co-ordinates are available on request from the Cambridge Crystallographic Data Centre.*

5-*Methyl*-2-(4-*methylpent*-4-*enoyl*)*cyclopentanone* (**26**).—Following the procedure used for the 1,3-dione (**20**), acylation of 4-(5-methylcyclopent-1-enyl) morpholine (13.30 g) with 4-methylpent-4-enoyl chloride (10.48 g), gave the 1,3-*dione* (7.12 g, 46.1%) as a pale yellow liquid, b.p. 86—92 °C/0.5 mmHg; $\nu_{max.}$ 1 740, 1 703, 1 665, and 1 607 cm^{-1}; δ_H 4.75—4.67 (m, $=CH_2$), 3.55—3.36 (m, OCCHCO), 3.11—2.93 (m, 1 H), 2.76—2.08 (m, 8 H), 1.76 and 1.74 (m, MeC=), and 1.16—1.06 (m, Me); δ_C 214.1, 213.6, 206.6, 203.9, 203.4, 178.6, 144.3, 110.6 (t), 110.2 (t), 109.0, 61.7 (d), 61.3 (d), 44.6 (t), 44.4 (t), 42.4 (t), 41.4 (t), 41.0 (t), 33.2 (t), 32.9 (t), 31.1 (t), 31.0 (t), 30.0 (t), 29.9 (t), 29.1 (t), 23.9 (q), 22.7 (t), 22.6 (t), 22.4 (t), 15.3 (q), 14.4 (q), and 13.9 (q) p.p.m.[34] (Found: *m/z* 194.1311. $C_{12}H_{18}O_2$ requires *M*, 194.1307).

5-*Methyl*-2-[4-*methyl*-1-(*dimethyl-t-butylsilyloxy*)*pent*-4-*enylidene*]*cyclopentanone* (**27**).—Dry triethylamine (5.16 ml) was added dropwise to a rapidly stirred solution of the 1,3-dione (**26**) (2.16 g) and dimethyl t-butylsilyl chloride (3.70 g) in dry benzene (200 ml) under nitrogen. The mixture was stirred at 60 °C for 12 h, then cooled and quickly filtered under suction. The precipitate of triethylamine hydrochloride was washed with dry hexane (3 × 40 ml) and the combined filtrates were then evaporated. The pale yellow residue was taken up in dry hexane (150 ml), then filtered and re-evaporated to give the *silyl ether* (3.31 g, 96.5%) as a pale yellow liquid which was used without further purification; $\nu_{max.}$ 1 705 and 1 645 cm^{-1}; δ_H 4.57 (m, $=CH_2$), 2.8—1.31 (m, 9 H), 1.60 (m, MeC=), 1.15 (d, *J* 7 Hz, Me), 0.88 (Me_3CSi), 0.14 (Me_2Si); δ_C 207.8, 164.2, 144.7, 117.5, 110.3 (t), 45.5 (d), 35.8 (t), 31.5 (t), 28.6 (t), 25.9 (t), 25.7 (3 × q), 22.3 (q), 18.3, 15.0 (q), −3.5 (q), −3.6 (q) p.p.m.

1-*Isopropylidene*-3a-*methyl*-4a-(*dimethyl-t-butylsilyloxy*)-2,3,3a,4,4a,5,6,7-*octahydrocyclobuta*[1,2:1,4]*dicyclopentene* (**29**).—Lithium wire (0.90 g) and titanium(III) chloride (5.74 g) were slurried in dry DME (60 ml) under an argon atmosphere, and the stirred mixture was then heated under reflux for 1 h. The black slurry was cooled to room temperature and a solution of the photoadduct (**17c**) (291.2 mg) in dry acetone (0.54 ml) added

* For details see para. 5.6.3 in 'Instructions for Authors,' *J. Chem. Soc., Perkin Trans. 1*, 1988, Issue 1.

over 4 h with the aid of a motor-syringe. The mixture was stirred at room temperature for 0.5 h and then at reflux for 12 h. After being cooled to room temperature, the mixture was diluted with pentane (80 ml) and filtered under suction through a pad of Florisil. The residue was washed with pentane (2 × 80 ml) and then decomposed by slow dropwise addition of methanol, until gas evolution ceased. The resulting black coloured solution was filtered under suction through a pad of Florisil, and the filter pad was then washed with an excess of pentane. The combined filtrates were washed successively with water (200 ml) and brine (200 ml), then dried, and evaporated to leave a pale green oil which was chromatographed on Silica gel G using pentane as eluant to give the *alkene* (239.8 mg, 75.6%) as a colourless oil: $\nu_{max.}$ 1 250 and 1 080 cm^{-1}; δ_H 2.40—1.56 (m, 12 H), 1.69 (d, *J* 1.6 Hz, MeC=), 1.64 (d, *J* 1.5 MeC=), 0.93 (Me), 0.86 (Me_3CSi), 0.04 (MeSi), 0.02 (MeSi); δ_C 139.1, 123.2, 82.3, 62.7, 47.0 (t), 42.0 (t), 41.4 (t), 40.9, 32.3 (t), 30.9 (t), 25.8 (3 × q), 24.8 (t), 22.9 (q), 22.5 (q), 20.9 (q), 17.9, −2.5 (q), and −2.9 (q) p.p.m. (Found: *m/z* 320.2519. $C_{20}H_{36}OSi$ requires *M*, 320.2536).

1-*Isopropyl*-3a-*methyl*-2,3,3a,4,7,8-*hexahydroazulen*-5(6H)-*one* (**15**).—Aqueous hydrofluoric acid (40%, 7.5 ml) was added in one portion to a stirred solution of the alkene (**29**) (320.6 mg) in THF (17 ml). After being stirred at room temperature for 1.5 h, the mixture was heated at 60 °C for 2.5 h, then cooled, poured into aqueous sodium hydroxide (2M, 90 ml), and extracted with ether (3 × 50 ml). The combined extracts were then washed with brine (70 ml), dried and evaporated to give an orange oil (280.0 mg) which was chromatographed on Silica gel G using ether–light petroleum (b.p. 40—60 °C) (1:1) as eluant to give the azulenone[22] (128.5 mg, 62.3%) as an almost colourless oil; $\nu_{max.}$ 1 695 cm^{-1}; δ_H 2.6—2.72 (m, CHC=), 2.54 (2 H, 4-H), 2.38—2.45 (m, 2 H, 6-H), 2.15—2.28 (m, 2 H), 2.02—1.86 (m, CH_2C=), 1.85—1.52 (m, 6 H), 1.01 (Me), and 0.97 and 0.94 (each d, *J* 6.8 Hz, 11- and 12-H_3); δ_C 212.8, 142.1, 138.7, 55.1 (t), 47.7, 43.9 (t), 38.3 (t), 27.4 (t), 26.8 (d), 24.9 (t), 24.3 (q), 24.0 (t), 21.5 (q), and 21.1 (q) p.p.m. (Found: C, 81.6; H, 11.2%; *m/z* 206.1677. $C_{14}H_{22}O$ requires C, 81.5; H, 10.75%; *M*, 206.1671).

(3aα,6β)-*Isopropyl*-3a,6-*dimethyl*-2,3,3a,4,7,8-*hexahydroazulen*-5(6H)-*one* (**34**).—Butyl-lithium solution (1.25M in hexane, 0.66 ml) was added dropwise to a stirred solution of hexamethyldisilazide (0.17 ml) in dry THF (3 ml) under nitrogen at −10 °C. After being stirred at −10 °C for 1 h, the solution was cooled to −78 °C, and a solution of the bicycle (**15**) (155 mg) in dry THF (1 ml) added dropwise. The solution was stirred at −78 °C for a further hour, and then a solution of dry methyl iodide (0.06 ml) in dry THF (1 ml) was added. The stirred mixture was allowed to warm slowly to room temperature over 14 h, and was then quenched by the addition of water (10 ml), and extracted with ether (3 × 20 ml). The combined extracts were washed successively with aqueous hydrochloric acid (2M, 10 ml), saturated aqueous sodium hydrogen carbonate (10 ml), and brine (10 ml). Evaporation of the dried extracts gave a pale yellow oil, which was chromatographed on Silica gel G using ether–light petroleum (b.p. 40—60 °C) (1:4) as eluant to give the *methylated bicycle* (145.0 mg, 87.5%, eluted second) as an almost colourless oil; $\nu_{max.}$ 1 700 cm^{-1}; δ_H 2.58 (m, CHC=), 2.53—2.45 (m, C*H*Me), 2.52 (d, *J* 15 Hz, β-C*H*HCO), 2.48 (d, *J* 15.1 Hz, α-CH*H*CO), 2.17 (m, CH_2C=), 2.00—1.55 (m, 6 H), 1.01 (d, *J* 6.8 Hz, β-Me), 0.99 (Me), 0.96 (d, *J* 6.8 Hz, Me), 0.91 (d, *J* 6.9 Hz, Me); δ_C 213.5, 141.5, 139.3, 53.3 (t), 48.5 (d), 47.3, 37.2 (t), 34.6 (t), 27.4 (t), 26.8 (d), 25.2 (q), 23.4 (t), 21.6 (q), 21.1 (q), and 17.3 (q) p.p.m. (Found: *m/z* 220.1826. $C_{15}H_{24}O$ requires *M*, 220.1825); together with the *bismethylated bicycle* (19.7 mg, eluted first) as a colourless oil; $\nu_{max.}$ 1 695 cm^{-1}; δ_H 2.63 (m, CHC=), 2.59—2.46 (m, 1 H), 2.58 (d, *J* 16.9 Hz, β-CH*H*CO), 2.54 (d, *J* 16.9 Hz, α-C*H*HCO), 2.18 (m, CH_2C=), 1.96—1.83 (m, 2 H), 1.70—1.50 (m, 3 H), 1.08 (α-Me), 1.01 (β-Me), 0.98 (Me), 0.96 (d, *J* 6.1 Hz, Me), 0.91 (d, *J* 6.8 Hz, Me); δ_C 215.5, 141.4, 138.2, 51.8 (t), 48.3, 47.3, 38.5 (t), 38.4 (t), 27.7 (t), and 26.7 (d), 25.7 (q), 25.2 (q), 24.5 (q), 21.4 (q), 21.1 (t), and 21.0 (q) p.p.m. (Found: *m/z* 234.1980. $C_{16}H_{26}O$ requires *M*, 234.1982).

(3aα,6β)-1-*Isopropyl*-3a-*methyl*-6-(5-*trimethylsilylpent*-4-*ynyl*)-2,3,3a,4,7,8-*hexahydroazulen*-5(6H)-*one* (**32b**).—A solution of the bicycle (**15**) (77.0 mg) in dry THF (1.0 ml) was added dropwise to a stirred solution of lithium hexamethyldisilazide (1M in THF, 0.4 ml) in dry THF (3 ml), containing hexamethylphosphoramide (1 ml), under nitrogen at −15 °C. After being stirred at −15 °C for 30 min, the solution was allowed to warm to room temperature, and then stirred at room temperature for 1 h. The solution was re-cooled to −15 °C, and a solution of the trimethylsilyl analogue of the iodo-alkyne (**31**) (120 mg) in dry THF (1 ml) added dropwise. The stirred mixture was allowed to warm slowly to room temperature over 12 h, then quenched by the addition of water (10 ml), and extracted with ether (3 × 20 ml). The combined extracts were washed successively with aqueous hydrochloric acid (2M, 10 ml), saturated aqueous sodium hydrogen carbonate solution (10 ml), and brine (10 ml). Evaporation of the dried extracts gave a pale yellow oil, which was chromatographed on Silica gel G using ether–light petroleum (b.p. 40—60 °C) (1:9) as eluant to give the *alkylated bicycle* (88.3 mg, 68.7%) as a colourless oil; $\nu_{max.}$ 2 190 and 1 695 cm^{-1}; δ_H 2.65—2.49 (m, CHC=), 2.50 (d, *J* 12.3 Hz, β-C*H*HCO), 2.45 (d, *J* 12.3 Hz, α-CH*H*CO), 2.49—2.35 (m, CHCO), 2.30—2.11 (m, CH_2C= and CH_2C=), 2.09—1.08 (m, 10 H), 0.97 (Me), 0.94 and 0.91 (each d, *J* 6.9 Hz, 11- and 12-H_3), and 0.13 (Me_3Si); δ_C 213.3, 141.5, 139.5, 107.2, 84.7, 53.9 (t), 53.7 (d), 47.4, 37.6 (t), 32.5 (t), 31.5 (t), 27.4 (t), 26.8 (d), 26.4 (t), 25.0 (q), 23.4 (t), 21.6 (q), 21.1 (q), 19.9 (t), and 0.18 (3 × q) p.p.m. (Found: *m/z* 344.2519. $C_{22}H_{36}OSi$ requires *M*, 344.2533).

1-*Isopropyl*-3a-*methyl*-2′-*methylene*-2,3,3a,4,7,8-*hexahydrospiro*[*azulene*-6,1′-*cyclopentan*]-5(6H)-*one* (**37**).—A solution of the ketone (**32b**) (227 mg) in dry DME (1 ml) was added to a stirred suspension of oil-free sodium hydride (10 mg) and methyl iodide (400 μl) in dry DME (3 ml), and the mixture stirred under nitrogen at 80 °C for 3 h. On being cooled, the mixture was quenched by the addition of dilute hydrochloric acid (2M, 10 ml), and then extracted with ether (3 × 20 ml). The combined extracts were washed successively with saturated aqueous sodium hydrogen carbonate (10 ml) and brine (10 ml). Evaporation of the dried extracts gave the crude product which was chromatographed on Silica gel HF 254 using ether–light petroleum (b.p. 40—60 °C) (1:9) as eluant to give the *spiroketone* (82.8 mg, 46.0%) as an almost colourless oil; $\nu_{max.}$ 1 695 and 1 652 cm^{-1}; major isomer (3aα,6*R**)-δ_H 4.96 (m, =C*H*H), 4.82 (m, =CH*H*), 2.89 (d, *J* 10.7 Hz; β-C*H*HCO), 2.33 (d, *J* 9.5 Hz, α-CH*H*CO), 2.66—2.50 (m, CHC=), 2.48—2.21 (m, 6 H), 2.09—1.35 (m, 8 H), 0.99 (d, *J* 6.6 Hz, Me), 0.89 (d, *J* 7.3 Hz, Me), and 0.85 (Me); δ_C 211.8, 157.8, 139.9 (2 × s), 106.8 (t), 62.8, 53.9 (t), 48.8, 39.0 (t), 38.1 (t), 36.3 (t), 34.5 (t), 27.7 (t), 26.6 (d), 23.6 (t), 23.3 (q), 21.9 (t), 21.6 (q), and 21.1 (q) p.p.m.; minor isomer (3aα,6*S**)-δ_H 4.92 (m, =C*H*H), 4.81 (m, =CH*H*), 3.06 (d, *J* 11.3 Hz, β-C*H*HCO), 2.45 (d, *J* 11.5 Hz, α-CH*H*CO), 2.66—2.50 (m, CHC=), 2.48—2.21 (m, 6 H), 2.09—1.35 (m, 8 H), 0.99 (d, *J* 6.6 Hz, Me), 0.89 (d, *J* 7.3 Hz, Me), and 0.85 (Me); δ_C 211.5, 157.2, 143.9, 135.2, 106.2 (t), 60.9, 52.1 (t), 48.9, 37.8 (t), 34.7 (2 × t), 34.1 (t), 28.0 (t), 26.9 (d), 26.1 (q), 23.5 (t), 21.9 (t), 21.6 (q), and 21.1 (q) p.p.m. (Found: *m/z* 272.2150. C, 83.3; H, 10.7%. $C_{19}H_{28}O$ requires *M*, 272.2139; C, 83.8; H, 10.4%).

5-(*Tri-isopropylsilyl*)*pent*-4-*yn*-1-*ol*.—Butyl-lithium solution (1.58M in hexane, 3.2 ml) was added to a stirred solution of pent-

4-ynol (4.25 g) in dry THF (200 ml) at 0 °C under nitrogen. The solution was allowed to warm to room temperature over 30 min, then cooled to 0 °C where trimethylsilyl chloride (6.35 ml) was added. The solution was again allowed to warm to room temperature, and then stirred for 1 h, before re-cooling to 0 °C. Butyl-lithium solution (1.58M in hexane, 32 ml) was added, and the mixture was stirred at 0 °C for 30 min, and then at room temperature for 1 h. Tri-isopropylsilyl chloride (10.0 g) was added, and the mixture was stirred at room temperature for 16 h. The mixture was quenched by the addition of aqueous hydrochloric acid (2M, 80 ml), and then extracted with ether (3 × 75 ml). Evaporation of the dried ether extracts left a residue consisting of a 4:1 mixture of tri-isopropylsilyl- and trimethylsilyl-pentynols. The residue was taken up in methanol (200 ml), potassium hydroxide (2.0 g) was added, and the mixture was then stirred at room temperature for 2 h. The mixture was neutralized with 2M aqueous hydrochloric acid, the methanol was evaporated, and the residue was dissolved in water (100 ml); the mixture was then extracted with ether (3 × 80 ml), and the combined extracts washed with brine (100 ml). Evaporation of the dried extracts followed by distillation of the residue gave the *alcohol* (4.91 g, 40.4%) as a colourless liquid, b.p. 128 °C/0.5 mmHg; $\nu_{max.}$ 3 300 and 2 160 cm^{-1}; δ_H 3.72 (t, *J* 6 Hz, CH_2OH), 2.32 (t, *J* 7 Hz, CH_2C=), 1.97 (OH), 1.70 (dt, *J* 7 and 6 Hz, CH_2), and 0.92 (Pr^i_3Si) [Found: *m/z* 197.1383 ($M - C_3H_7$). $C_{14}H_{28}OSi$ requires $M - C_3H_7$, 197.1362].

5-*Methanesulphonyloxy*-1-(*tri-isopropylsilyl*)*pent*-1-*yne*.—Methanesulphonyl chloride (0.9 ml) was added to a stirred solution of 5-(tri-isopropylsilyl)pent-4-yn-1-ol (2.47 g) in dry dichloromethane (30 ml), containing a 50% molar excess of triethylamine (4.17 ml) under nitrogen at −10 °C. The mixture was stirred at −10 °C for 30 min then transferred to a pre-cooled separating funnel and treated successively with ice-cold water (10 ml), cold aqueous hydrochloric acid (2M, 10 ml), saturated aqueous sodium hydrogen carbonate solution (10 ml), and brine (10 ml). Evaporation of the dried organic phase gave the *methanesulphonate* (3.2 g, 98%) as a pale yellow liquid which was used without further purification; $\nu_{max.}$ 2 180, 1 355, and 1 175 cm^{-1}; δ_H 4.42 (t, *J* 6 Hz, CH_2OMs), 3.04 (3 H, MeS), 2.46 (t, *J* 7 Hz, CH_2C=), 1.97 (dt, *J* 7 and 6 Hz, CH_2), and 1.08 (Pr^i_3Si).

5-*Iodo*-1-(*tri-isopropylsilyl*)*pent*-1-*yne* (**31**).—A suspension of 5-methanesulphonyloxy-1-(tri-isopropylsilyl)pent-1-yne (3.27 g) and sodium iodide (3.10 g) in acetone (120 ml) was stirred at room temperature for 12 h, and then heated under reflux for a further 2 h. After being cooled, the sodium mesylate which had formed was removed by filtration, and the filtrate was then evaporated. The residue was taken up in pentane (100 ml) and then re-filtered. Evaporation of the filtrate followed by distillation of the residue gave the *iodo-alkyne* (3.24 g, 90.5%) as a colourless liquid, b.p. 125—127 °C/0.3 mmHg; $\nu_{max.}$ 2 175 and 880 cm^{-1}; δ_H 3.37 (t, *J* 7 Hz, CH_2I), 2.44 (t, *J* 6.4 Hz, CH_2C=), 2.02 (dt, *J* 7 and 6.5 Hz, CH_2), and 1.08 (Pr^i_3Si) (Found: *m/z* 350.0920. $C_{14}H_{27}ISi$ requires *M*, 350.0925).

(3aα,6β)-1-*Isopropyl*-6-(5-*tri-isopropylsilylpent*-4-*ynyl*)-3a-*methyl*-2,3,3a,4,7,8-*hexahydroazulen*-5(6H)-*one* (**32a**).—A solution of the bicycle (**15**) (161.0 mg) in dry THF (1 ml) was added dropwise to a stirred solution of lithium hexamethyldisilazide (1M in THF, 0.85 ml) in dry THF (7 ml), containing hexamethylphosphoramide (HMPA) (0.14 ml), under nitrogen at −10 °C. After being stirred at −10 °C for 20 min, the solution was allowed to warm to room temperature where it was stirred for 1 h. The solution was re-cooled to −10 °C, and a solution of the iodo-pentyne (**31**) (281.6 mg) in dry THF (1 ml) was then added dropwise. The stirred mixture was allowed to warm slowly to room temperature over 12 h, and then quenched with water (15 ml), and extracted with ether (3 × 20 ml). The combined extracts were washed successively with aqueous hydrochloric acid (2M, 10 ml), saturated aqueous sodium hydrogen carbonate solution (10 ml), and brine (10 ml). Evaporation of the dried extracts left a pale yellow oil, which was chromatographed on Silica gel HF254 using ether–light petroleum (b.p. 40—60 °C) (1:9) as eluant to give the *alkylated bicycle* (105.8 mg, 31.6%, eluted first) as a colourless oil; $\nu_{max.}$ 2 180 and 1 695 cm^{-1}; δ_H 2.59 (m, CHC=), 2.50 (d, *J* 16.3 Hz, β-C*H*HCO), 2.46 (d, *J* 16.3, α-CH*H*CO), 2.40—2.34 (m, CHCO), 2.26—2.14 (m, CH_2C= and $CH_2C\equiv$), 2.07—1.93 (m, 1 H), 1.81—1.44 (m, 9 H), 1.05 (Pr^i_3Si), 0.97 (Me), and 0.96 and 0.91 (each d, *J* 6.8 Hz, 11- and 12-H_3); δ_C 213.4, 141.4, 139.5, 108.7, 80.5, 54.0 (d), 53.6 (t), 47.7, 37.6 (t), 32.6 (t), 31.5 (t), 27.4 (t), 26.8 (d), 26.6 (t), 24.9 (q), 23.4 (t), 21.6 (q), 21.1 (q), 19.9 (t), 18.7 (6 × q), and 11.4 (3 × d) p.p.m. (Found: *m/z* 428.3479. $C_{28}H_{48}OSi$ requires *M*, 428.3473), together with recovered starting material (63.0 mg, eluted second).

(3aα,6S*)-1-*Isopropyl*-6-(5-*tri-isopropylsilylpent*-4-*ynyl*)-3a,6-*dimethylazulen*-5(6H)-*one* (**33**).—A solution of the ketone (**32a**) (121.0 mg) in dry DME (1 ml) was added to a stirred suspension of oil-free sodium hydride (7.5 mg) and methyl iodide (250 μl) in dry DME (3 ml), and the mixture stirred under nitrogen at room temperature for 24 h. A second equivalent of sodium hydride (7.5 mg) was added and the mixture was stirred for a further 24 h. The mixture was quenched by the addition of water (15 ml), extracted with ether (3 × 15 ml) and the combined extracts washed with brine (10 ml), and then dried. Evaporation of the solvent left a residue which was chromatographed on Silica gel HF254 to give the *methylated bicycle* (73 mg, 58%) as a colourless oil, consisting of a 4:1 mixture of *S**- and *R**-epimers by n.m.r. analysis; $\nu_{max.}$ 2 180 and 1 695 cm^{-1}; major isomer (3aα,6*S**)-δ_H 2.81 (d, *J* 11 Hz, β-C*H*HCO), 2.67—2.42 (m, CHC= and 10β-H), 2.30 (d, *J* 17.5 Hz, α-CH*H*CO), 2.30—2.08 (m, CH_2=, $CH_2C\equiv$, 9α-, and 10α-H), 1.85—1.38 (m, 7 H), 1.05 (Pr^i_3Si), 1.04 (13-H_3), 0.95, (14-H_3), and 0.94 and 0.89 (each d, *J* 6.8 Hz, 11- and 12-H_3); minor isomer (3aα.6*R**)-δ_H 2.72 (d, *J* 10.7 Hz, β-C*H*HCO), 2.67—2.42 (m, CHC= and 10β-H), 2.33 (d, *J* 10.7 Hz, α-CH*H*CO), 2.30—2.08 (m, CH_2C= and $CH_2C\equiv$), 1.85—1.38 (m, 9 H), 1.06 (13-H_3), 1.05 (Pr^i_3Si), 0.95 (14-H_3), and 0.94 and 0.89 (each d, *J* 6.8 Hz, 11- and 12-H_3) (Found: *m/z* 442.3625. $C_{29}H_{50}OSi$ requires *M*, 442.3629).

(3aα,6S*)-1-*Isopropyl*-3a,6-*dimethyl*-6-(5-*pent*-4-*ynyl*)-2,3,3a,4,7,8-*hexahydroazulen*-5(6H)-*one* (**14**).—Tetrabutylammonium fluoride (1 ml in THF, 300 μl) was added to a solution of the ketone (**33**) (13.5 mg) in dry THF (1 ml) and the mixture was stirred under nitrogen at room temperature for 2 min. Water (5 ml) was added, and the mixture was then extracted with ether (3 × 10 ml). Evaporation of the dried extracts gave the crude acetylenic ketone which was chromatographed on Silica gel HF254 using ether-hexane (1:10) as eluant to give the *acetylenic ketone* (6.3 mg, 72.4%) as a colourless oil, consisting of a 5:1 mixture of *S**- and *R**-epimers by n.m.r. analysis; $\nu_{max.}$ 3 265 and 1 695 cm^{-1}; major isomer (3aβ,6*S**)-δ_H 2.81 (d, *J* 11.1 Hz, β-C*H*HCO), 2.60 (qq, *J* 6.7 and 6.7 Hz, CHC=), 2.49 (t, *J* 7.3 Hz, 10β-H), 2.32 (d, *J* 11.1 Hz, α-CH*H*CO), 2.21—2.00 (m, CH_2C=, $CH_2C\equiv$, 9α-H, and 10α-H), 1.95 (t, *J* 2.5 Hz, =CH), 1.85—1.39 (m, 7 H), 1.04 (13-H_3), 0.95 (14-H_3), 0.94 (d, *J* 6.7 Hz, Me), and 0.89 (d, *J* 6.9 Hz, Me); δ_C 214.8, 142.5, 136.9, 84.0, 68.6 (d), 51.5 (t), 49.7, 48.2, 38.2 (t), 37.7 (t), 35.6 (t), 27.7 (t), 26.8 (d), 25.4 (q), 23.2 (t), 21.3 (q), 21.2 (2 × q), 20.8 (t), and 19.0 (t) p.p.m.; minor isomer (3aβ,6*R**) (**35**)-δ_H 2.66 (d, *J* 10.7 Hz, β-C*H*HCO), 2.70—2.37 (m, CHC= and 10β-H), 2.42 (d, *J* 10.7 Hz, α-C*H*HCO), 2.28—2.09 (m, CH_2C= and $CH_2\equiv$), 1.94 (t, *J* 2.7 Hz, ≡CH); 1.91—1.38 (m, 9 H), 1.06 (13-H_3), 0.96

(14-H_3), 0.94 (d, *J* 6.7 Hz, Me), 0.91 (d, *J* 6.8 Hz, Me); δ_C 214.9, 140.7, 139.2, 84.1, 68.5 (d), 52.5 (t), 51.8, 48.4, 38.9 (t), 38.6 (t), 37.1 (t), 27.8 (t), 26.6 (d), 23.9 (q), 23.2 (t), 21.5 (q), 21.4 (q), 21.1 (q), 20.6 (t), and 19.0 (t) p.p.m. (Found: *m/z* 286.2298. $C_{20}H_{30}O$ requires *M*, 286.2296).

The (3aβ,6*R**)-azulenone (**35**) was also produced (62%) from (3aα,6β)-1-isopropyl-3a,6-dimethyl-2,3,3a,4,7,8-hexahydroazulenone (**34**) following deprotonation (LDA, THF) and alkylation of the resulting enolate with 5-iodopent-1-yne.

(3aα,4aα,8aβ)-1-*Isopropyl*-3a,8a-*dimethyl*-5-*methylene*-2,3,3a,4,4a,7,8,8a,9,10-*decahydro*-6H-*benz*[f]*azulen*-4a-*ol* (**38**).—Treatment of a solution of the acetylenic ketone (**14**) (64.4 mg) in dry THF (10 ml) with a solution of sodium naphthalene radical anion (0.6M in THF, 0.95 ml) by the general procedure,[9] followed by a modified work-up procedure in which the combined extracts were also washed with 10% silver nitrate solution (20 ml), gave the crude alcohol (320 mg). Column chromatography on Silica gel HF254 eluting first with pentane (2.5 solvent lengths) and then with ether–hexane (1:10) gave the *alcohol* (26.5 mg, 41.0%) as a colourless oil; $\nu_{max.}$($CHCl_3$) 3 450 and 1 640 cm^{-1}; δ_H 4.81 (t, *J* 1.52 Hz, =CH), 4.76 (m, =CH), 2.60 (qq, *J* 6.9 and 6.8 Hz, CHC=), 2.57—2.44 (m, 6α-, 9α-, and 10β-H), 2.34—2.10 (m, 2-H_2, 8α- and 10α-H), 2.11 (d, *J* 14.5 Hz, 4β-H), 2.10—1.41 (m, 8 H), 1.48 (d, *J* 14.6, 4α-H), 1.35 (3a-Me), 0.94 and 0.92 (each d, *J* 6.79, 11- and 12-H_3), and 0.78 (8a-Me); δ_C 154.0, 138.9 (2 × s), 108.3 (t), 78.9, 50.9, 47.7 (t), 43.0 (t), 41.8, 38.2 (t), 32.1 (t), 31.8 (t), 27.4 (t), 26.8 (d and q), 22.8 (t), 22.5 (t), 21.3 (q), 20.4 (q), and 17.7 (q) p.p.m. (Found: *m/z* 288.2455. $C_{20}H_{32}O$ requires *M*, 288.2453).

(3aα,4aα6α,8aβ)-1-*Isopropyl*-3a,8a-*dimethyl*-5-*methylene*-6H-2,3,3a,4,4a,7,8,8a,9,10-*decahydrobenz*[f]*azulene*-4a,6-*diol* (*Isoamijiol*) (**1**).—t-Butyl hydroperoxide (70% solution in water, 175 μl) was added to a stirred solution of the alcohol (**38**) (23.5 mg), selenium dioxide (350 μg), and salicylic acid (2 mg) in dichloromethane (7 ml), and the solution was then stirred at room temperature for 3 h. The solution was diluted with benzene (5 ml) and then evaporated to a volume of approximately 3 ml, before it was diluted with ether (10 ml) and washed with aqueous potassium hydroxide solution (2M, 4 × 3 ml). Evaporation of the dried organic phase left a white residue which was subjected to preparative t.l.c. on Silica gel G plates, (85 × 31 × 0.25 mm), with hexane–acetone (2:1) as eluant to give a white solid (2 mg) consisting of isoamijiol, δ_H 5.08 (m, =CH), 5.01 (m, =CH), 4.29 (t, *J* 2.94 Hz, C*H*OH), 2.68—1.50 (m, 17 H), 1.34 (14-H_3), 0.94 and 0.92 (each d, *J* 6.6 Hz, 11- and 12-H_3), 0.77 (13-H_3), identical with an authentic sample, contaminated (~12%) with the *diene* (**39**) δ_H 5.57 (br t, 2-H), 5.43 (dd, *J* 4.6 and 9.6 Hz, 10-H), 4.34 (t, *J* 2.79 Hz, C*H*OH), 3.09 (dd, *J* 4.5 and 15.0 Hz, 9α-H), 2.68—1.50 (m, 16 H), 1.32 (14-H_3), 1.09 and 1.06 (each d, *J* 6.83 Hz, 11- and 12-H_3), and 0.83 (13-H_3) (Found: *m/z* 304.2407. $C_{20}H_{32}O_2$ requires *M*, 304.2402). No separation between compounds (**1**) and (**39**) could be achieved using medium pressure liquid chromatography, normal phase h.p.l.c., reverse phase h.p.l.c., or silver nitrate chromatography, with a wide range of solvent combinations and polarities.

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References

1 M. Ochi, *Suisangaku Shiriizu*, 1983, **45**, 101 (*Chem. Abstr.*, 1983, **99**, 20039j). See also: R. S. Jacobs, and S. White, and L. Wilson, *Fed. Proc., Fed. Am. Soc. Exp. Biol.*, 1981, **40**, 26.
2 (*a*) P. Crews, T. E. Klein, E. R. Hogue, and B. L. Myers, *J. Org. Chem.*, 1982, **47**, 811; (*b*) It is interesting to note that extracts containing dolastane diterpenes were used by Nero's mother, Agrippina, to poison his rivals during Nero's attempts to become Emperor of Rome. See: G. R. Pettit, R. H. Ode, C. L. Herald, R. B. Von Dreele, and C. Michel, *J. Am. Chem. Soc.*, 1976, **98**, 4677.
3 M. Ochi, M. Watanabe, I. Miura, M. Taniguchi, and T. Tokoroyama, *Chem. Lett.*, 1980, 1229; N. Harada, Y. Yokota, J. Iwabuchi, H. Uda, and M. Ochi, *J. Chem. Soc., Chem. Commun.*, 1984, 1220; see also: H. H. Sun, O. J. McConnell, W. Fenical, K. Hirotsu, and J. Clardy, *Tetrahedron*, 1981, **37**, 1237.
4 M. Ochi, M. Watanabe, M. Kido, Y. Ichikawa, I. Miura, and T. Tokoroyama, *Chem. Lett.*, 1980, 1233; M. Ochi, I. Miura, and T. Tokoroyama, *J. Chem. Soc., Chem. Commun.*, 1981, 100.
5 Full summary and bibliography see: M. Kaisin, J. C. Braekman, D. Daloze, and B. Tursch, *Tetrahedron*, 1985, **41**, 1067.
6 A. F. Halim, A. M. Zaghloul, C. Zdero, and F. Bohlmann, *Phytochemistry*, 1983, **22**, 1510 and refs. therein.
7 A. J. Barker and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1885; A. J. Barker, M. J. Begley, M. Mellor, D. A. Otieno, and G. Pattenden, *ibid.*, 1983, 1893; M. J. Begley, M. Mellor, and G. Pattenden, *ibid.*, 1983, 1905, and earlier refs. cited therein.
8 A. J. Barker and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1983, 1901; A. M. Birch and G. Pattenden, *ibid.*, 1983, 1913, and earlier refs. cited therein.
9 G. Pattenden and G. M. Robertson, *Tetrahedron Lett.*, 1983, **24**, 4617; *Tetrahedron*, 1985, **41**, 4011.
10 G. Pattenden and S. J. Teague, *Tetrahedron Lett.*, 1982, **23**, 5471; *J. Chem. Soc., Perkin Trans. 1*, 1988, preceding paper; M. Ladlow, G. Pattenden, and S. J. Teague, *Tetrahedron Lett.*, 1986, **27**, 3279.
11 Preliminary communication: G. Pattenden and G. M. Robertson, *Tetrahedron Lett.*, 1986, **27**, 399.
12 L. M. Browne, R. E. Klinck, and J. B. Stothers, *Org. Magn. Reson.*, 1979, **12**, 561; W. A. Ayer, L. M. Browne, S. Fung, and J. B. Stothers, *ibid.*, 1978, **11**, 73; L. M. Browne, R. E. Klinck, and J. B. Stothers, *Can. J. Chem.*, 1979, **57**, 803.
13 G. Stork, A. Brizzolara, H. Landexsman, J. Szmuszkovicz, and R. Terrel, *J. Am. Chem. Soc.*, 1963, **85**, 207.
14 C. A. Grob and A. Waldner, *Helv. Chim. Acta*, 1979, **62**, 1854.
15 H. Seto, S. Hirokawa, Y. Fujimoto, and T. Tatsuno, *Chem. Lett.*, 1983, 989.
16 *cf.* J. S. H. Kueh, M. Mellor, and G. Pattenden, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1052, and refs. therein.
17 *cf.* G. Pattenden and S. J. Teague, *Tetrahedron Lett.*, 1984, **25**, 3021; L. F. Tietze and U. Reichert, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 830.
18 (*a*) Y. Inubushi, T. Kikuchi, T. Ibuka, K. Tanaka, I. Saji, and K. Tokane, *J. Chem. Soc., Chem. Commun.*, 1972, 1251; Y. Inubushi, T. Tikuchi, T. Ibuka, K. Tanaka, I Saji, and K. Tokane, *Chem. Pharm. Bull.*, 1974, **22**, 349; (*b*) J. N. Marx and L. R. Norman, *Tetrahedron Lett.*, 1973, 4375; J. N. Marx and L. R. Norman, *J. Org. Chem.*, 1975, **40**, 1602, and; (*c*) J. A. Marshall and G. M. Cohen, *J. Org. Chem.*, 1971, **36**, 877.
19 For an example see: M. C. Pirrung, *J. Am. Chem. Soc.*, 1979, **101**, 7130.
20 (*a*) J. B. Conant and A. H. Blatt, *J. Am. Chem. Soc.*, 1929, **51**, 1227; (*b*) F. C. Whitemore and R. S. George, *ibid.*, 1942, **64**, 1239, and; (*c*) D. O. Cowan and H. S. Mosher, *J. Org. Chem.*, 1962, **27**, 1.
21 J. E. McMurry, M. P. Fleming, K. L. Kees, and L. R. Krepski, *J. Org. Chem.*, 1978, **43**, 3255; J. E. McMurry and L. R. Krepski, *ibid.*, 1976, **41**, 3929.
22 H. Wolf, M. Kolleck, and W. Rascher, *Chem. Ber.*, 1976, **109**, 2805.
23 See: M. R. Roberts and R. H. Schlessinger, *J. Am. Chem. Soc.*, 1979, **101**, 7626, and; G. J. Quallich and R. H. Schelessinger, *ibid.*, 1979, **101**, 7627.
24 See: A. Antony and T. Maloney, *J. Org. Chem.*, 1972, **37**, 1055.
25 S. C. Welch and R. L. Walters, *J. Org. Chem.*, 1974, **39**, 2665. See also: S. C. Welch and M. E. Walters, *ibid.*, 1978, **43**, 2715.
26 *cf.* W. P. Jackson and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 1981, 1516.
27 M. Christl and J. D. Roberts, *J. Org. Chem.*, 1972, **37**, 3443.

28 For a related example see: E. J. Corey M. Behforouz, and M. Ishiguro, *J. Am. Chem. Soc.*, 1979, **101**, 1608.
29 See for example: (*a*) H. Schostarez and L. A. Paquette, *Tetrahedron*, 1981, **37**, 4431; (*b*) E. R. Kroft and A. B. Smith III, *J. Org. Chem.*, 1984, **49**, 832.
30 For a review of this type of reaction see: J. M. Conia and P. Le Perchec, *Synthesis*, 1975, 1.
31 *cf.* C. Eaborn and D. R. M. Walton, *J. Organomet. Chem.*, 1965, **4**, 217.
32 For comparative data used to establish the structure of (**39**) see ref. 3.
33 G. Pattenden and S. J. Teague, *J. Chem. Soc., Perkin Trans. 1*, 1988, preceding paper.
34 J. R. Carruthers, 'CRYSTALS User Manual,' Oxford University Computing Laboratory, 1975.
35 P. Main, S. L. Fiske, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, 'MULTAN' A System of Computer Programs for the Automatic Solution of Crystal Structures from *X*-ray Diffraction Data,' University of York, England, and Louvain, Belgium, 1980.

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