An Efficient Synthesis of Functionalized Tricyclo[6.3.1.$0^{1,6}$]dodec-4-enes by a Stereoselective Intramolecular Diels–Alder Reaction ‡

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An efficient and highly stereoselective synthesis of functionalized tricyclo[6.3.1.$0^{1,6}$]dodec-4-enes (**1c,e,f—h**), which would be useful and common synthons for constructing basic carbon frameworks of various kinds of natural products, is described. The key feature of the synthesis was a stereoselective intramolecular Diels–Alder reaction of the cyclohexanone derivatives (**10c,e,f—h**), which were easily derived from cyclohexanone in 4—5 steps. The whole structure and the stereochemistry of a major cycloadduct (**1e**) was established by a single-crystal *X*-ray analysis.

In recent years much attention has been focussed on the intramolecular Diels–Alder reaction [2] for assembling complex polycyclic molecular structures in a single step. In connection with our current studies directed towards total synthesis of complex natural products using an intramolecular Diels–Alder reaction,[3] we planned to synthesize 2-substituted 6αH-tricyclo[6.3.1.$0^{1,6}$]-dodec-4-en-12-ones (**1**),† as promising synthons for constructing the basic carbon frameworks of some natural products, by this cycloaddition.

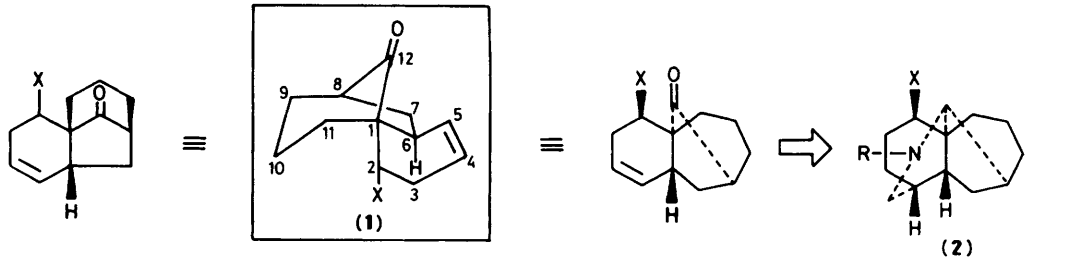
The target molecule has the suitably positioned functionality for assembling not only the ABEF ring system (**2**) of the aconitine-type alkaloid cardiopetaline [4] (**3**) but also the basic skeleton of the sesquiterpenoid α-cedrene [5] (**4**) and of the diterpenoid stemodin (**5**).[6] In this paper we describe in detail an efficient and stereoselective synthesis of the tricyclic ketone (**1**) and the stereochemical aspects of a novel type of intramolecular Diels–Alder reaction.‡

Results and Discussion

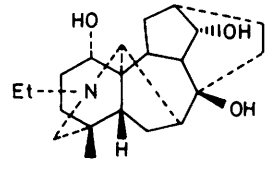
The substrates for an intramolecular Diels–Alder reaction, the cyclohexanone derivatives (**10a—h**), were prepared from cyclohexanone by a route of sequential Claisen rearrangement, formylation, and substitution with sulphur functionalities or acyloxy groups. Thus, reaction of the divinylcarbinol (**7**),[7] prepared from ethyl formate and vinylmagnesium bromide, with an excess of 1-methoxycyclohexene (**6**),[8] easily derivable from

† All compounds reported in this paper are racemic. For convenience, only one enantiomer is shown.

‡ During the course of this study, a similar type of intramolecular Diels–Alder reaction applied to the total synthesis of quadrone was independently reported by two groups of workers (R. H. Schlessinger, J. L. Wood, A. P. Poss, R. A. Nugent, and W. H. Parsons, *J. Org. Chem.*, 1983, **48**, 1146; J. M. Dewanckele, F. Zutterman, and M. Vandewalle, *Tetrahedron*, 1983, **39**, 3235).



a; X = SBu^n
b; X = $S(O)Bu^n$
c; X = $S(O)_2Bu^n$
d; X = SPh
e; X = $S(O)_2Ph$
f; X = OAc
g; X = OCOPh
h; X = $OCOPr^i$



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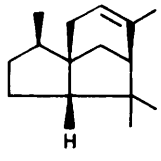

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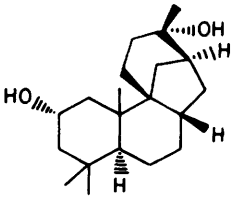

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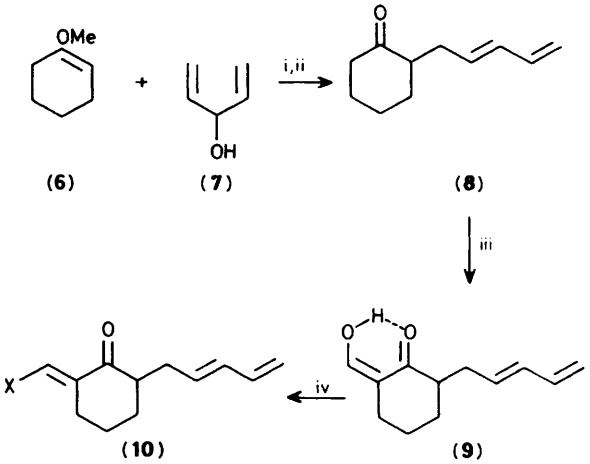
Table 1. Thermolysis of the cyclohexanones (**10a—e**)

Entry	X	Solvent	Reaction temp. (°C)	Reaction time (h)	Product	Product yield (%)	Isomer ratio
1	SBu^n	mesitylene	240	30			
2	$S(O)Bu^n$	toluene	180	30			
3	$S(O)_2Bu^n$	toluene	180	17	(**1c**) + (**11c**)	75	5.6:1[a]
4	SPh	mesitylene	200	30			
5	$S(O)_2Ph$	toluene	180	14	(**1e**) + (**11e**)	72	3.4:1

[a] Determined by h.p.l.c.

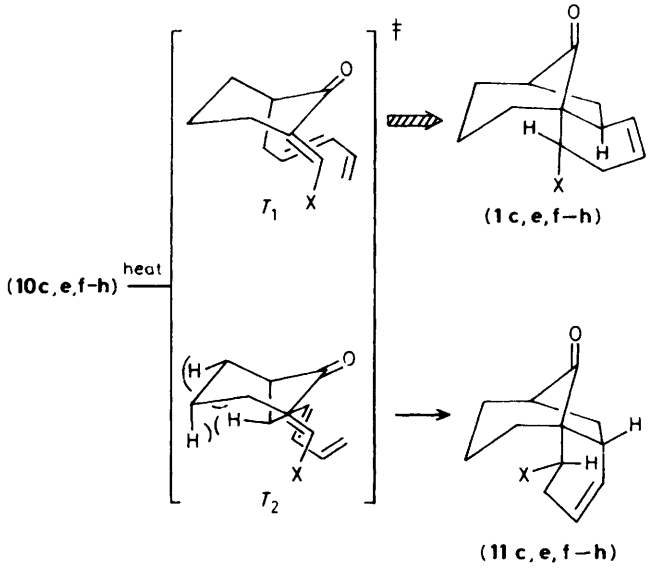
cyclohexanone, in the presence of a catalytic amount of mercury(II) acetate at 120 °C for 24 h, followed by further heating with a catalytic amount of camphor-10-sulphonic acid at the same temperature for 20 h, gave 2-(penta-2,4-dienyl)-cyclohexanone (**8**) *via* Claisen rearrangement.[9] The crude compound (**8**) was then treated with ethyl formate and sodium hydride as base to afford the hydroxymethylene ketone (**9**) in 80% overall yield from (**6**). Attachment of the dienophilic portions onto compound (**9**) could be achieved easily by standard procedures as shown in Scheme 1, affording compounds (**10a—h**). The configuration of the dienophile enone in (**10a—h**) was identical from ^1H n.m.r. and/or ^{13}C n.m.r. spectra and was assigned as *E* from the chemical shift[10] of the β-proton of the enone [for (**10c,e**): δ_H 6.68 (1 H, m); for (**10f**): δ_H 7.98 (1 H, t, *J* 2 Hz)].



a; X = SBu^n
b; X = $S(O)Bu^n$
c; X = $S(O)_2Bu^n$
d; X = SPh
e; X = $S(O)_2Ph$
f; X = OAc
g; X = OCOPh
h; X = $OCOPr^i$

Scheme 1. *Reagents:* i, $Hg(OAc)_2$, NaOAc; ii, CSA; iii, NaH, HCO_2Et, benzene; iv, **a**: Bu^nSH, *p*-TsOH, benzene; **b**: (**10a**), MCPBA (1.5 equiv.), CH_2Cl_2; **c**: (**10a**), MCPBA (2 equiv.) CH_2Cl_2; **d**: MsCl, Et_3N, DMAP then PhSNa; **e**: (**10d**), $(NH_4)_6MO_7O_{24}\cdot 4H_2O$, 30% H_2O_2, aq. EtOH; **f**: Ac_2O, pyridine, DMAP, CH_2Cl_2; **g**; $(PhCO)_2O$, pyridine, DMAP, CH_2Cl_2; **h**: $(Pr^iCO)_2O$, pyridine, DMAP, CH_2Cl_2

The key intramolecular Diels–Alder reaction of the trienones (**10a—e**) was conducted in a *ca.* 50 mmol solution in toluene or mesitylene using a sealed tube.* The results of the cycloadditions were summarized in Table 1. The cycloaddition was expected to produce predominantly compound (**1**) with the desired stereochemistry on the basis of the obvious relative steric congestion of the transition state T_2 over T_1 (Scheme 2).



Scheme 2.

Although no detectable cycloadducts could be obtained in the thermolysis of the sulphides (**10a,d**) and the sulphoxide (**10b**), the sulphones (**10c,e**), prepared from the oxidation of (**10a**) with 2 mol equiv. of *meta*-chloroperbenzoic acid (MCPBA) or of (**10d**) with hydrogen peroxide in the presence of ammonium molybdate,[11] were thermolysed at 180 °C to give the cycloadducts as a mixture of two diastereoisomers in 75 and 62% yield, respectively.

At this point, however, the ^1H n.m.r. spectroscopic data of the cycloadducts showed little characteristic information about the structure. The whole structure and the stereochemistry of the major cycloadduct (**1e**) was therefore unambiguously established by a single-crystal *X*-ray analysis (Figure).†

Two cycloadducts (**1e**) and (**11e**)‡ thus obtained were the diastereoisomers at C-6, which could be supported by the fact that a mixture of (**1e**) and (**11e**), when treated with lithium in liquid ammonia in the presence of ethanol followed by

* Although the Lewis acid [Et_2AlCl, $AlCl_3$, or $B(OMe)_3$]-catalysed cyclization was also examined under various conditions, no cycloadducts could be obtained.

† Monoclinic, space group $P2_1/c$ with a = 9.945(4), b = 12.234(2), c = 16.216(6) Å; β = 126.58(2)°; D_c = 1.33 g cm^{-3}, Z = 4. Final R value was 0.0461. Details will be reported elsewhere.

‡ The suffix letters **a**—**h** for compounds (**11**) and (**16**) refer to the substituents shown for structures (**1**) and (**10**).

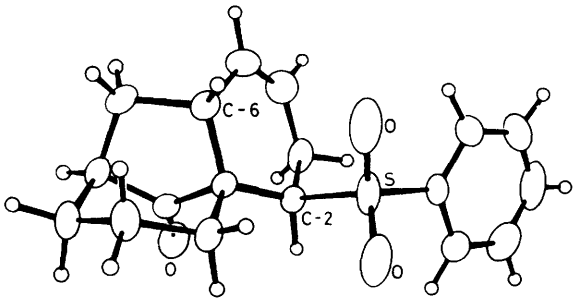
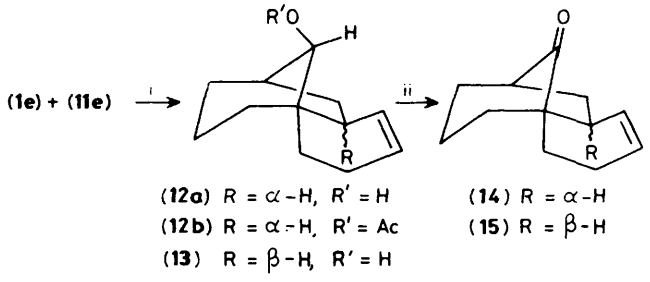


Figure. Projection drawing of the tricyclic ketone (**1e**)

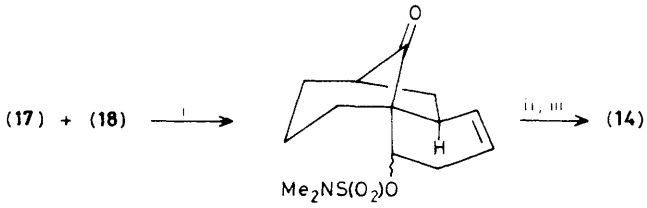
oxidation [with pyridinium chlorochromate (PCC)] of the resulting alcohols (**12a** and **13**), gave two ketones (**14**) and (**15**) (Scheme 3). Interestingly, the Birch reduction of the keto sulphone (**1e**) afforded selective formation of a single alcohol (**12a**). The configuration of the C-12 hydroxy group could be confirmed as axial on the basis of a vicinal coupling (with 1-H) of the equatorial proton at C-12 at δ_H 4.80 as a doublet with J 5.0 Hz in the ^{1}H n.m.r. spectrum of compound (**12b**).



Scheme 3. *Reagents:* i, Li, liq. NH_3, EtOH; ii, PCC, CH_2Cl_2

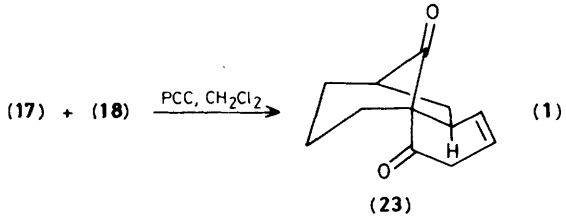
In order to improve the stereoselectivity of the cycloaddition, thermolysis of the substrates with an acyloxy group on a dienophilic entity was examined. The results of the cycloaddition are summarized in Scheme 4 and Table 2. The thermolysis was conducted on a mesitylene solution in a sealed tube at 220 °C, and four possible alcohols (**17**), (**18**), and (**19**) (about two chiral centres at C-2 and C-6) could be detected after basic hydrolysis of the crude cycloadducts (**16f—h**). Despite the homogeneity of the starting trienones (**10f—h**), the occurrence of an epimerization at C-2 might be explainable by an equilibration *via* a retro-Diels–Alder reaction and re-addition under such considerably harsher thermal conditions (at 220 °C for 38—60 h). Another possibility for the epimerization, retro-aldol reaction and re-addition sequence during basic treatment of the cycloadducts (**16f—h**), is excluded by the fact that the crude cycloadduct (**16f—h**) could be detected by t.l.c. as a mixture of four components.

The stereochemistry at C-6 in the major two isomers (**17**) and (**18**) was established by their conversion into the enone (**14**) (Scheme 5). Namely, a mixture of alcohols (**17**) and (**18**) was



Scheme 5. *Reagents:* i, SO_2Cl_2, pyridine then Me_2NH; ii, Na, liq. NH_3, MeOH, THF; iii, PCC, CH_2Cl_2

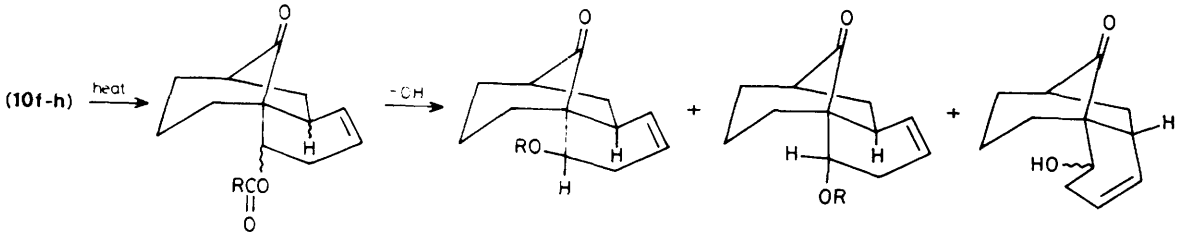
treated under Umezawa's[12] conditions for deoxygenation, followed by oxidation with PCC, to give the enone (**14**) which was found to be identical with authentic material prepared *via* Scheme 3. Furthermore, the mixture of compounds (**17**) and (**18**) was oxidized with PCC to afford the same diketone (**23**) as a single product, indicating that compounds (**17**) and (**18**) were epimeric at C-2 [reaction (1)].



Concerning the configuration at C-2 in alcohols (**17**) and (**18**), the hydroxy group in (**17**) could be considered as β-oriented from the ^{1}H n.m.r. spectrum of the corresponding methyl ether (**20**), derived from alcohol (**17**) by a standard methylation, in which the α-proton at C-2 was observed at δ_H 3.40 as a triplet with J 2.0 Hz. On the other hand, that proton of

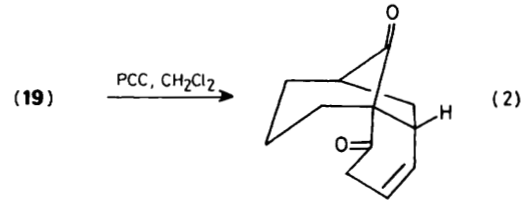
Table 2. Thermolysis of the cyclohexanones (**10f—h**)

Entry	Reaction time (h)	Product	Product yield (%)	Isomer ratio (**17**):(**18**):(**19**)
1	50	(**16f**)	47	12.0:2.6:1
2	38	(**16g**)	40	2.7:2.1:1
3	60	(**16h**)	50	12.4:7.7:1

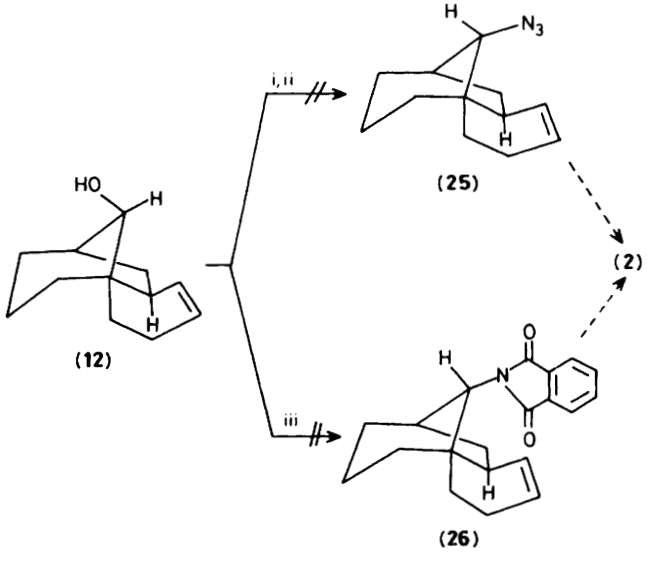


Scheme 4.

methyl ether (**21**), derived from alcohol (**18**), appeared at δ_H 3.08 as a double doublet with J 6.0 and 10.0 Hz, indicating that compound (**18**) is the α-hydroxy isomer. The other cycloadduct (**19**), an inseparable mixture of two diastereoisomers, was oxidized with PCC to give a single diketone (**24**) which was completely different from the diketone (**23**) derived from the major adducts [reaction (2)]. The observation revealed that the minor adduct (**19**) should be one diastereoisomer at C-6 and a diastereoisomeric mixture at C-2.



With the tricyclic enol (**12**) constructed efficiently, we then turned our attention to the problem of constructing the ABEF ring system (**2**) of aconitine-type diterpene alkaloids. The strategy envisioned introduction of the amino functionality into C-12 with equatorial orientation, in order to construct the F ring with a C-4 olefin, utilizing an S_N2-type reaction of compound (**12**). This approach appeared to be reasonable; however, no displacement [13] could be induced even under various conditions such as standard mesylation of the alcohol (**12**) followed by displacement with azide, or by a Mitsunobu reaction [14] of (**12**) with phthalimide as indicated in Scheme 6. Further experiments aimed at assembling the ring system (**2**) by other strategies are in progress.



Scheme 6. *Reagents:* i, $CH_3S(O)_2Cl$, pyridine; ii, NaN_3, DMF; iii, Ph_3P, EtO_2C–N=N–CO_2Et, phthalimide, THF

In conclusion, despite the lower yield of the cycloadducts than in the case of sulphones, higher stereoselectivity [14.6:1 for (**10f**) and 20.1:1 for (**10h**)] with respect to the configuration at C-6 was achieved in the intramolecular Diels–Alder reaction of compounds (**10f,h**), and it was also found that the presence of the sp^3 carbon adjacent to the carbonyl group on the dienophilic portion would be necessary for increased stereoselectivity of the cycloaddtion. Thus, we could develop an efficient and highly stereoselective route for constructing the functionalized tricyclo[6.3.1.$0^{1,6}$]dodec-4-ene system by using a novel type of intramolecular Diels–Alder reaction as the key step.

Experimental

General Methods.—M.p.s were determined on a Yanaco micro melting point apparatus and are uncorrected. I.r. spectra were recorded on a Hitachi 260-10 spectrophotometer. N.m.r. spectra were measured on JEOL JNM-PMX-60 and JEOL PS-100 spectrometers. Chemical shifts are reported as δ_H values relative to internal $SiMe_4$. Mass spectra were taken on a Hitachi M-52G spectrometer and JEOL-TMS-OISG-2 spectrometer. All reactions were carried out under dry nitrogen. Column chromatography was carried out with silica gel (Wako gel C-200). The phrase 'residue upon work-up' refers to the residue when the organic layer was separated, dried over $MgSO_4$, and the solvent was evaporated under reduced pressure. All new compounds described in this Experimental section were homogeneous on t.l.c.

1-*Methoxycyclohexene* (**6**).—To a vigorously stirred mixture of cyclohexanone (99.78 g, 1.02 mol) and trimethyl orthoformate (129.46 g, 1.22 mol) was added toluene-*p*-sulphonic acid monohydrate (PTSA) (2.10 g, 0.01 mol) in portions at 0 °C. After being stirred for 24 h at room temperature, the mixture was distilled at atmospheric pressure to give 1-methoxycyclohexene (**6**) (105.99 g, 93%) as an oil, b.p. 128—138 °C (lit.,[8] 138—142 °C); $\nu_{max.}$(neat) 1 675 cm^{-1} (enol ether); δ_H (60 MHz; $CDCl_3$) 3.48 (3 H, s, OMe), and 4.50 (1 H, m, olefinic H); m/z 112 (M^+).

Penta-1,4-dien-3-ol (**7**).—To a stirred mixture of magnesium (19.93 g, 0.82 g-atom), anhydrous tetrahydrofuran (THF) (100 ml), and anhydrous ether (50 ml) was added dropwise a solution of vinyl bromide (91.02 g, 0.85 mol) in anhydrous THF (100 ml) and a solution of ethyl formate (16.42 g, 0.22 mol) in anhydrous ether (100 ml) at the same time. After being stirred at room temperature for 30 min and at 40 °C for 3 h, the reaction mixture was treated with saturated aqueous ammonium chloride at 0 °C and the inorganic precipitate was filtered off on Celite. The residue upon work-up was distilled to give the carbinol (**7**) (14.21 g, 60%) as an oil, b.p. 90—115 °C (lit.,[7] 115—116 °C); $\nu_{max.}$(neat) 3 075—3 650 cm^{-1} (OH); δ_H (60 MHz; CCl_4) 3.69 (1 H, br s, OH), 4.33—4.80 (1 H, m, >C*H*OH), and 4.94—6.16 (6 H, m, olefinic H).

2-(*Penta-2,4-dienyl*)*cyclohexanone* (**8**).—To a mixture of 1-methoxycyclohexene (**6**) (69.45 g, 619 mmol) and penta-1,4-dien-3-ol (**7**) (17.36 g, 206 mmol) were added mercury(II) acetate (4.60 g, 14 mmol) and sodium acetate (1.69 g, 21 mmol) and the mixture was refluxed for 24 h. After the mixture had cooled, it was diluted with ether and filtered. The ethereal solution was washed successively with water and saturated aqueous sodium chloride. The residue upon work-up was used in the next reaction without further purification.

To the crude product was added a catalytic amount of camphor-10-sulphonic acid (CSA) and the mixture was refluxed again for 20 h, then concentrated under reduced pressure. The residual crude products were chromatographed with n-hexane–ethyl acetate (95:5 v/v) as eluant to afford the *ketone* (**8**) (25.36 g, 75%) as an oil, $\nu_{max.}$(neat) 1 710 cm^{-1} (C=O); δ_H (60 MHz; CCl_4) 4.67—6.50 (5 H, m, olefinic H) (Found: M^+, 164.1219. $C_{11}H_{16}O$ requires M, 164.1202).

2-(*n-Butylthiomethylene*)-6-(*penta-2,4-dienyl*)*cyclohexanone* (**10a**).—To a suspension of sodium hydride (60% in oil; 1.24 g, 31.0 mmol) in anhydrous benzene (40 ml) was added a solution

of the ketone (**8**) (1.27 g, 7.7 mmol) in anhydrous benzene (20 ml) at room temperature and the mixture was stirred for 1 h at the same temperature. To the mixture was added dropwise ethyl formate (2.29 g, 30.9 mmol) and, after being stirred for 24 h at room temperature, the mixture was treated with water at 0 °C, and the organic phase was extracted with 10% aqueous sodium hydroxide. The combined aqueous layers were washed with ether, acidified with 10% aqueous sulphuric acid, and extracted with ether. The extracts were washed with saturated aqueous sodium chloride, and the residue upon work-up gave the unstable hydroxymethylene compound (**9**) as a brown oil which was used in the next reaction without further purification.

To a stirred solution of the crude hydroxymethylene compound (**9**) (580 mg, 3.0 mmol) in anhydrous benzene (15 ml) were added a catalytic amount of PTSA, and butane-1-thiol (760 mg, 8.4 mmol). After being refluxed for 1 h, the mixture was diluted with saturated aqueous sodium hydrogen carbonate and extracted with ether, and the extracts were washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed with n-hexane–ethyl acetate (95:5 v/v) as eluant to afford the *n-butylthiomethylene derivative* (**10a**) (590 mg, 74%) as a yellow oil, $\nu_{max.}$(neat) 1 660 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$) 4.80—6.50 (5 H, m, olefinic H) and 7.52 (1 H, t, *J* 2.0 Hz, =C*H*SBu^n); δ_C (25 MHz; $CDCl_3$) 13.562 (q, CH_3), 21.546 (t), 27.887 (t), 28.180 (t), 32.643 (t), 34.051 (t), 34.287 (t), 47.966 (d, C-6), 115.129 (t, C-11), 130.807 (s, C-2), 132.685 (d), 132.859 (d), 136.969 (d), 142.314 (d, C-12), and 197.502 p.p.m. (s, C-1) (Found: M^+, 264.1530. $C_{16}H_{24}OS$ requires *M*, 264.1546).

2-(*Penta*-2,4-*dienyl*)-6-*phenylthiomethylenecyclohexanone* (**10d**).—To a solution of the crude hydroxymethylene compound (**9**) (4.36 g, 22.7 mmol), anhydrous triethylamine (9.18 g, 90.7 mmol), and a catalytic amount of 4-dimethylaminopyridine (DMAP) was added dropwise methanesulphonyl chloride (5.20 g, 45.4 mmol) at 0 °C and the mixture was stirred at room temperature. After being stirred for 30 min, the mixture was treated with sodium thiophenolate (6.59 g, 49.9 mmol) and was then stirred for 2 h at the same temperature. The insoluble material was filtered off with suction and the filtrate was concentrated. The residue was chromatographed with chloroform–n-hexane (1:1 v/v) as eluant to afford the *phenylthiomethylene derivative* (**10d**) (3.19 g, 50%) as a yellow oil, $\nu_{max.}$(neat) 1 660 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$) 4.80—6.50 (5 H, m, olefinic H) and 7.63 (1 H, t, *J* 2.0 Hz, =C*H*SPh); δ_C (25 MHz; $CDCl_3$) 16.849 (t, C-4), 28.180 (t, C-5), 28.298 (t, C-3), 33.993 (t, C-7), 48.259 (d, C-6), 115.246 (t, C-11), 127.989 (s, C-2), 129.163 (d), 129.280 (d), 130.689 (d), 132.507 (d), 132.997 (d), 136.912 (d), 140.139 (d), 142.723 (d, C-12), and 197.850 p.p.m. (s, C-1) (Found: M^+, 284.1223. $C_{18}H_{20}OS$ requires *M*, 284.1233).

Oxidation of Sulphide (**10a**).—*Preparation of sulphoxide* (**10b**). To a solution of the n-butyl sulphide (**10a**) (0.11 g, 0.4 mmol) in anhydrous methylene dichloride (2 ml) was added MCPBA (70%; 0.14 g, 0.6 mmol) at −78 °C. After being stirred at the same temperature for 5 min, the reaction mixture was diluted with saturated aqueous sodium hydrogen carbonate and the organic layer was separated. The aqueous layer was extracted with methylene dichloride and the combined extracts were washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed with benzene–ethyl acetate (2:1 v/v) as eluant to afford 2-(*n-butylsulphinylmethylene*)-6-(*penta*-2,4-*dienyl*)*cyclohexanone* (**10b**) (0.09 g, 74%) as an oil, $\nu_{max.}$(neat) 1 690 (C=O) and 1 030 cm^{-1} (SO); δ_H (100 MHz; $CDCl_3$) 4.80—6.48 (5 H, m, olefinic H) and 6.72 [1 H, m, =C*H*S(O)Bu^n] (Found: M^+, 280.1500. $C_{16}H_{24}O_2S$ requires *M*, 280.1497).

Oxidation of Sulphide (**10a**).—*Preparation of sulphone* (**10c**). To a solution of the n-butyl sulphide (**10a**) (1.44 g, 5.4 mmol) in anhydrous methylene dichloride (40 ml) was added MCPBA (70%; 2.08 g, 11.4 mmol) at −10 °C. After being stirred at the same temperature for 1 h, the reaction mixture was diluted with saturated aqueous sodium hydrogen carbonate and the organic layer was separated. The aqueous layer was extracted with chloroform and the combined extracts were washed successively with water and saturated aqueous sodium chloride. The residue upon work-up was chromatographed with n-hexane–ethyl acetate (9:1 v/v) as eluant to give 2-(*n-butylsulphonylmethylene*)-6-(*penta*-2,4-*dienyl*)*cyclohexanone* (**10c**) (0.83 g, 51%) as an unstable yellow oil, $\nu_{max.}$(neat) 1 692 (C=O), and 1 295 and 1 123 cm^{-1} (SO_2); δ_H (100 MHz; $CDCl_3$) 4.80—6.46 (5 H, m, olefinic H) and 6.68 [1 H, m, =C*H*S(O)$_2$Bu] (Found: M^+, 296.1449. $C_{16}H_{24}O_3S$ requires *M*, 296.1446).

Oxidation of Sulphide (**10d**).—*Method A*. A solution of the phenyl sulphide (**10d**) (280 mg, 0.98 mmol) in anhydrous methylene dichloride (17 ml) was treated with MCPBA (70%; 400 mg, 2.19 mmol) and worked up similarly. The crude products were chromatographed with n-hexane–ethyl acetate (7:3 v/v) as eluant to afford 2-(*penta*-2,4-*dienyl*)-6-*phenylsulphonylmethylenecyclohexanone* (**10e**) (81.4 mg, 26%) as an unstable yellow oil, $\nu_{max.}$(neat) 1 695 (C=O) and 1 300 and 1 123 cm^{-1} (SO_2); δ_H (100 MHz; $CDCl_3$) 4.72—6.38 (5 H, m, olefinic H) and 6.68 (1 H, dd, *J* 1.0 and 2.0 Hz, =C*H*SO$_2$Ph) (Found: M^+, 316.1157. $C_{18}H_{20}O_3S$ requires *M*, 316.1132).

Method B. To an ethanol (65 ml)–water (13.5 ml) solution of the phenyl sulphide (**10d**) (1.46 g, 5.1 mmol) was added 30% aqueous hydrogen peroxide (13.5 ml) and 0.1M-aqueous ammonium molybdate (9.7 ml), and the mixture was stirred for 3 h at room temperature. The excess of hydrogen peroxide was decomposed by addition of manganese dioxide at 0 °C and the mixture was then stirred for 15 min. After most of ethanol had been removed under reduced pressure, the solid mass was filtered through Celite, washed with chloroform, and the aqueous layer was extracted with chloroform. The combined organic solutions were washed with saturated aqueous sodium chloride and the residue upon work-up was chromatographed with n-hexane–ethyl acetate (4:1 v/v) as eluant to give the phenyl sulphone (**10e**) (0.97 g, 60%), which was identical with the authentic material prepared by Method A.

2-*Acetoxymethylene*-6-(*penta*-2,4-*dienyl*)*cyclohexanone* (**10f**).—A solution of the crude hydroxymethylene compound (**9**) (84 mg, 0.44 mmol) in anhydrous methylene dichloride (2.0 ml) was treated with acetic anhydride (49 mg, 0.48 mmol), anhydrous pyridine (41 mg, 0.52 mmol), and a catalytic amount of DMAP at room temperature for 12 h. After removal of the solvent, anhydrous n-hexane was added to the residue and the insoluble material was filtered off. Distillation of the solvent gave, as a residue, the *acetate* (**10f**) (90 mg, 88%) as an unstable brown oil, $\nu_{max.}$($CHCl_3$) 1 770 and 1 690 (C=O) and 1 620 cm^{-1} (diene); δ_H (100 MHz; $CDCl_3$) 2.20 (3 H, s, $COCH_3$), 4.72—6.48 (5 H, m, olefinic H), and 7.98 (1 H, t, *J* 2.0 Hz, =C*H*OAc); δ_C (25 MHz; $CDCl_3$) 20.665 (q, CH_3), 21.722 (t, C-4), 24.599 (t, C-5), 28.356 (t, C-3), 33.465 (t, C-7), 49.081 (d, C-6), 115.307 (t, C-11), 132.216 (d), 133.038 (s, C-2), 136.852 (d), 140.905 (d), 141.079 (d, C-12), 166.972 (s, C-13), and 201.607 p.p.m. (s, C-1) (Found: M^+, 234.1260. $C_{14}H_{18}O_3$ requires *M*, 234.1257).

2-*Benzoyloxymethylene*-6-(*penta*-2,4-*dienyl*)*cyclohexanone* (**10g**).—A solution of hydroxymethylene (**9**) (3.21 g, 16.7 mmol) in anhydrous methylene dichloride (60 ml) was treated with benzoic anhydride (4.16 g, 18.4 mmol), anhydrous pyridine (1.59 g, 20.1 mmol), and a catalytic amount of DMAP at room temperature for 24 h. After removal of the solvent, the residue was chromatographed with n-hexane–ethyl acetate (95:5 v/v) as eluant to give the *benzoate* (**10g**) (3.55 g, 70%) as an unstable

yellow oil, $\nu_{max.}$($CHCl_3$) 1 750 and 1 690 (C=O) and 1 600 cm^{-1} (diene); δ_H 100 MHz; $CDCl_3$) 4.80—6.50 (5 H, m, olefinic H), 7.30—7.76 (3 H, m, ArH), and 7.80—8.28 (3 H, m, ArH and =C*H*OBz); δ_C (25 MHz; $CDCl_3$) 21.722 (t, C-4), 24.775 (t, C-5), 28.415 (t, C-3), 33.523 (t, C-7), 49.140 (d, C-6), 115.364 (t, C-11), 128.693 (s, C-14), 130.102 (s, C-2), 133.094 (d), 134.095 (d), 136.912 (d), 141.314 (d, C-12), 162.623 (s, C-13), and 201.551 p.p.m. (s, C-1) (Found: M^+, 296.1402. $C_{19}H_{20}O_3$ requires *M*, 296.1412).

2-*Isobutyryloxymethylene*-6-(*penta*-2,4-*dienyl*)*cyclohexanone* (**10h**).—A solution of the hydroxymethylene compound (**9**) (130 mg, 0.68 mmol) in anhydrous methylene dichloride (5.0 ml) was treated with isobutyric anhydride (120 mg, 0.74 mmol), anhydrous pyridine (60 mg, 0.81 mmol), and a catalytic amount of DMAP at room temperature for 3 h. After removal of the solvent, anhydrous n-hexane was added to the residue and the insoluble material was filtered off. Removal of the solvent from the filtrate gave the *isobutyrate* (**10h**) (170 mg, 96%) as an unstable brown oil, $\nu_{max.}$($CHCl_3$) 1 760 and 1 690 (C=O) 1 605 cm^{-1} (diene); δ_H (100 MHz; $CDCl_3$) 1.24 (6 H, d, *J* 7.0 Hz, CH*Me*$_2$), 4.80—6.50 (5 H, m, olefinic H), and 7.99 (1 H, m, =C*H*OCOPr^i); δ_C (25 MHz; $CDCl_3$) 18.669 (q, CH_3), 21.722 (t, C-4), 24.599 (t, C-5), 28.415 (t, C-3), 33.582 (t, C-7), 49.081 (d, C-14), 115.364 (t, C-11), 121.704 (s, C-2), 132.272 (d), 133.094 (d), 136.912 (d), 141.314 (d, C-12), 173.135 (s, C-13), and 201.729 p.p.m. (s, C-1) (Found: M^+, 262.1559. $C_{16}H_{22}O_3$ requires *M*, 262.1567).

General Procedure for Thermolysis of the Sulphones (**10c**) *and* (**10e**).—A solution of the sulphone (**10c**, **10e**) in anhydrous degassed toluene was heated at 180 °C in the presence of a catalytic amount of Methylene Blue[15] in a sealed tube.

2α-(*n-Butylsulphonyl*)*tricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**1c**) *and* (**11c**).—The thermolysis of compound (**10c**) (760 mg, 2.56 mmol) in anhydrous toluene (76.0 ml) was conducted for 17 h. After removal of the solvent, the residue was chromatographed with n-hexane–ethyl acetate (4:1 v/v) as eluant to give the tricyclododecenone (**1c**) and (**11c**) (570 mg, 75%), an inseparable C-6 epimeric mixture, as a solid, m.p. 56—61 °C (Found: C, 64.85; H, 8.05. $C_{16}H_{24}O_3S$ requires C, 64.85; H, 8.15%); $\nu_{max.}$($CHCl_3$) 1 740 (C=O) and 1 295 and 1 120 cm^{-1} (SO_2); δ_H (100 MHz; $CDCl_3$) 3.34 [0.15 H, dd, *J* 4.0 and 8.0 Hz, for (**11c**) 2-H], 3.44 [0.85 H, dd, *J* 3.0 and 6.0 Hz, for (**1c**) 2-H], and 5.35—5.72 (2 H, m, olefinic H); *m/z* 297 (M^+ + 1).

2α-*Phenylsulphonyltricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**1e**) *and* (**11e**).—The thermolysis of compound (**10e**) (640 mg, 2.02 mmol) in anhydrous toluene (64.0 ml) was conducted for 14 h. After removal of the solvent, the residue was chromatographed with n-hexane–ethyl acetate (17:3 v/v) as eluant to give the *cycloadduct* (**1e**) (310 mg, 48%) as needles after recrystallization from benzene–n-hexane, m.p. 144.5—145 °C (Found: C, 68.1; H, 6.4. $C_{18}H_{20}O_3S$ requires C, 68.3; H, 6.35%); $\nu_{max.}$($CHCl_3$) 1 735 (C=O) and 1 300 and 1 135 cm^{-1} (SO_2); δ_H (100 MHz; $CDCl_3$) 3.67 (1 H, dd, *J* 2.0 and 6.0 Hz, 2-H), 5.10—5.34 (1 H, m, olefinic H), and 5.56—5.80 (1 H, m, olefinic H); *m/z* 316 (M^+). From the later fractions, the minor *cycloadduct* (**11e**) (90 mg, 14%) was obtained as a yellow viscous oil, $\nu_{max.}$($CHCl_3$) 1 740 (C=O) and 1 300 and 1 140 cm^{-1} (SO_2); δ_H (100 MHz; $CDCl_3$) 3.66 (1 H, dd, *J* 8.0 and 10.0 Hz, 2-H), and 5.72 (2 H, br s, olefinic H) (Found: M^+, 316.1108. $C_{18}H_{20}O_3S$ requires *M*, 316.1133).

Tricyclo[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**14**) *and* (**15**).—To a stirred solution of liquid ammonia (10 ml) were added a *ca.* 1:1 mixture of the cycloadducts (**1e**) and (**11e**) (116 mg, 0.36 mmol) in anhydrous THF (1.0 ml), lithium (26 mg, 3.7 mg-atom), and anhydrous ethanol (5.0 ml) at −78 °C. After being stirred for 30 min at the same temperature, the reaction mixture was treated with an excess of ethanol, and the solvent was evaporated off. The residue was diluted with water, and the resulting mixture was extracted with ether. The extract was washed with saturated aqueous sodium chloride. The residue upon work-up gave a mixture of the alcohols (**12a**) and (**13**) (57 mg) as a brown oil which was used in the next reaction without further purification.

To a suspension of PCC (140 mg, 0.65 mmol) in anhydrous methylene dichloride (1.0 ml) was added in one portion a solution of the alcohols (**12a**) and (**13**) (57 mg) in anhydrous methylene dichloride (1.0 ml) and the mixture was further stirred at room temperature for 1 h. After addition of Florisil, the mixture was diluted with anhydrous ether and filtered through Celite. The filtrate was concentrated under reduced pressure and the residue was chromatographed with n-hexane–ethyl acetate (95:5 v/v) as eluant to afford 6α*H*-*tricyclo*-[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**14**) (13 mg, 20%) as an oil, $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$) 5.48 (2 H, br s, olefinic H) (Found: M^+, 176.1197. $C_{12}H_{16}O$ requires *M*, 176.1200). From the later fractions, 6β*H*-*tricyclo*[6.3.1.0^{1,6}]-*dodec*-4-*en*-12-*one* (**15**) (37 mg, 58%) was obtained as an oil, $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$) 5.44—5.92 (2 H, m, olefinic H) (Found: M^+, 176.1210).

6α*H*-12-anti-*Acetoxytricyclo*[6.3.1.0^{1,6}]*dodec*-4-*ene* (**12b**).—A mixture of the alcohol (**12a**) (150 mg, 0.47 mmol), anhydrous pyridine (1.0 ml), a catalytic amount of DMAP, and acetic anhydride (0.5 ml) was stirred at room temperature for 14 h. After removal of the solvent, the residue was chromatographed with chloroform–n-hexane (1:1) as eluant to give the *acetate* (**12b**) (84 mg, 45%) as an oil, $\nu_{max.}$($CHCl_3$) 1 730 cm^{-1} (ester); δ_H (100 MHz; $CDCl_3$) 2.10 (3 H, s, $OCOCH_3$), 4.80 (1 H, d, *J* 5.0 Hz, 12-H), and 5.50 (2 H, br s, olefinic H); δ_C (25 MHz; $CDCl_3$) 18.552 (t), 20.900 (t), 21.370 (q, CH_3), 24.716 (t), 28.650 (t), 32.760 (t), 33.641 (t), 35.343 (d, C-8), 38.044 (d, C-6), 41.038 (s, C-1), 73.740 (d, C-12), 123.879 (d), 132.155 (d), and 170.899 p.p.m. (s, C=O) (Found: M^+, 220.1462. $C_{14}H_{20}O_2$ requires *M*, 220.1462).

Thermolysis of the Acetate (**10f**).—A solution of the acetate (**10f**) (1.50 g, 6.4 mmol) and a catalytic amount of Methylene Blue in degassed anhydrous mesitylene (150 ml) was heated at 220 °C for 50 h in a sealed tube. After removal of the solvent, the cycloadduct (**16f**) (705 mg, 47%) was obtained as a brown oil which was used in the next reaction without further purification.

A solution of the cycloadduct (**16f**) (705 mg), a catalytic amount of tetrabutylammonium hydrogen sulphate, and lithium hydroxide monohydrate (490 mg, 11.7 mmol) in a mixture of methanol (12 ml)–methylene dichloride (4 ml)–water (4 ml) was stirred at room temperature for 11 h. After removal of methanol and methylene dichloride, the residue was diluted with water. The resulting mixture was extracted with chloroform and the extracts were washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed with n-hexane–ethyl acetate (4:1 v/v) as eluant to afford 6α*H*-2α-*hydroxytricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**18**) (50 mg, 4.1%) as an oil (Found: C, 75.2; H, 8.4. $C_{12}H_{16}O_2$ requires C, 75.0; H, 8.4%); $\nu_{max.}$($CHCl_3$) 3 530 (OH) and 1 720 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$) 3.30—3.70 (1 H, m, >C*H*OH) and 5.52 (2 H, m, olefinic H); *m/z* 192 (M^+). From the later fractions, 6β*H*-2-*hydroxytricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**19**) (1.9 mg, 1.5%), an inseparable epimeric mixture at C-2, was obtained as an oil, $\nu_{max.}$($CHCl_3$) 3 100—3 500 (OH) and 1 720 cm^{-1} (C=O); δ_H (100 MHz; $CDCl_3$) 3.80—4.28 (1 H, m, >C*H*OH) and 5.40—5.82 (2 H, m, olefinic H) (Found: M^+, 192.1147. $C_{12}H_{16}O_2$ requires *M*, 192.1149). From the last

fractions, 6α*H*-2β-*hydroxytricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**17**) (230 mg, 18.7%) was obtained as needles after recrystallization from benzene–n-hexane, m.p. 104.5—105 °C (Found: C, 74.8; H, 8.35. $C_{12}H_{16}O_2$ requires C, 74.95; H, 8.4%); $\nu_{max.}$(CHCl$_3$) 3 300—3 500 (OH) and 1 730 cm^{-1} (C=O); δ_H (100 MHz; CDCl$_3$) 3.98 (1 H, m, >C*H*OH) and 5.24—5.84 (2 H, m, olefinic H); *m*/*z* 192 (M^+).

Thermolysis of the Benzoate (**10g**).—The cycloadduct (**16g**) (219 mg, 40%) was obtained by heating a solution of the benzoate (**10g**) (547 mg, 1.85 mmol) in degassed anhydrous mesitylene (5.5 ml) at 220 °C for 38 h in a sealed tube, and which was submitted to the hydrolysis as described above without further purification to afford three products, (**17**) (62 mg, 17.5%), (**18**) (48 mg, 13.5%), and (**19**) (23 mg, 6.5%), which were identical with the authentic materials.

Thermolysis of the Isobutyrate (**10h**).—Thermolysis of the isobutyrate (**10h**) (622 mg, 2.37 mmol) in anhydrous mesitylene (100 ml) at 220 °C in a sealed tube for 60 h gave the cycloadduct (**16h**) (311 mg, 50%) which was submitted to the hydrolysis as described above without further purification to afford three products, (**17**) (32 mg, 7.0%), (**18**) (20 mg, 4.4%), and (**19**) (3 mg, 0.7%), which were also identical with the authentic materials.

Methylation of the Alcohol (**17**).—To a stirred suspension of sodium hydride (60% in oil; 52 mg, 1.30 mmol) in anhydrous dimethoxyethane (DME) (3.0 ml) was added a solution of the alcohol (**17**) (63 mg, 0.33 mmol) in DME (2.0 ml) at room temperature. After being stirred for 1 h, the mixture was treated with methyl iodide (231 mg, 1.63 mmol) and was then stirred for 12 h. The reaction mixture was quenched with saturated aqueous ammonium chloride and the most of DME was removed under reduced pressure. The residue was diluted with water, extracted with ether, and the extracts were washed with saturated aqueous sodium chloride. The residue upon work-up was chromatographed with n-hexane–ethyl acetate (7:3 v/v) as eluant to afford 6α*H*-2β-*methoxytricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**20**) (60 mg, 90%) as an oil, $\nu_{max.}$(CHCl$_3$) 1 730 (C=O) and 1 080 cm^{-1} (C–O–C); δ_H (100 MHz; CDCl$_3$) 3.20 (3 H, s, OCH$_3$), 3.40 (1 H, t, *J* 2.0 Hz, 2-H), and 5.20—5.90 (2 H, m, olefinic H) (Found: M^+, 206.1300. $C_{13}H_{18}O$ requires *M*, 206.1305).

Methylation of the Alcohol (**18**).—The same treatment of the alcohol (**18**) (23 mg, 0.12 mmol) with methyl iodide (84 mg, 0.59 mmol) in the presence of sodium hydride (60% in oil; 20 mg, 0.5 mmol) in anhydrous DME (2.0 ml) as above gave 6α*H*-2α-*methoxytricyclo*[6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**21**) (22 mg, 93%) as an oil (Found: C, 75.25; H, 9.05. $C_{13}H_{18}O_2$ requires C, 75.7; H, 8.8%); $\nu_{max.}$(CHCl$_3$) 1 730 (C=O) and 1 110 and 1 080 cm^{-1} (C–O–C); δ_H (100 MHz; CDCl$_3$) 3.08 (1 H, dd, *J* 6.0 and 10.0 Hz 2-H), 3.33 (3 H, s, OCH$_3$), and 5.42 (2 H, m, olefinic H); *m*/*z* 206 (M^+).

Alternative Preparation of 6α*H-Tricyclo*[6.3.1.0.^{1,6}]*dodec*-4-*en*-12-*one* (**14**).—To a cooled, stirred solution of a mixture of the alcohols (**17**) and (**18**) (10.8 mg, 0.056 mmol) in anhydrous methylene dichloride (0.5 ml) were added anhydrous pyridine (0.01 ml) and sulphuryl chloride (15.2 mg, 0.113 mmol) (ice–methanol–sodium chloride cooling bath). After the mixture had been stirred for 1 h at the same temperature, a solution of dimethylamine in methylene dichloride [from potassium carbonate (0.5 g), 50% aqueous dimethylamine (0.5 ml), and methylene dichloride (2.0 ml)] was added to the mixture which was then stirred for 6 h at room temperature. The mixture was diluted with 10% aqueous hydrochloric acid and extracted with chloroform. The extracts were dried over potassium carbonate. Removal of the solvent gave the *NN*-dimethylsulphamoyl compound (**22**) (19.8 mg) as a yellow oil, which was used in the following reaction without further purification.

To a stirred solution of the *NN*-dimethylsulphamoyl compound (**22**) (19.8 mg) in liquid ammonia (5 ml) and anhydrous THF (1 ml) was added a piece of sodium at −78 °C and the deep blue solution was kept for 1 h at the same temperature. Then, the mixture was treated carefully with an excess of dry methanol and the solvent was evaporated off. The residue was diluted with water and extracted with ether, and the extracts were washed with saturated aqueous sodium chloride. The residue upon work-up gave a crude oil, and this was taken up with anhydrous methylene dichloride (0.5 ml), and the solution was then treated with a suspension of PCC (20 mg, 0.09 mmol) in anhydrous methylene dichloride (0.5 ml) at room temperature for 1 h. After addition of Florisil, the mixture was diluted with anhydrous ether, and filtered through Celite. The filtrate was concentrated under reduced pressure and the residue was chromatographed with n-hexane–ethyl acetate (9:1 v/v) as eluant to afford 6α*H*-*tricyclo*(6.3.1.0^{1,6}]*dodec*-4-*en*-12-*one* (**14**) (3.0 mg, 30%), which was identical with the authentic material preprared from the sulphone (**1e**).

6α*H-Tricyclo*[6.3.1.0^{1,6}]*dodec*-4-*ene*-2,12-*dione* (**23**).—To a suspension of PCC (108 mg, 0.50 mmol) anhydrous methylene dichloride (0.5 ml) was added, in one portion, a solution of the mixture of alcohols (**17**) and (**18**) (48 mg, 0.25 mmol) in anhydrous methylene dichloride (1.0 ml) and the reaction mixture was stirred at room temperature for 3 h. After addition of Florisil, the mixture was diluted with anhydrous ether and filtered through Celite. The filtrate was concentrated under reduced pressure and the residue was chromatographed with n-hexane–ethyl acetate (17:3 v/v) as eluant to give the *diketone* (**23**) (21 mg, 44%) as an oil, $\nu_{max.}$(CHCl$_3$) 1 740 and 1 710 cm^{-1} (C=O); δ_H (60 MHz; CDCl$_3$) 5.72 (2 H, br s, olefinic H) (Found: M^+, 190.0990. $C_{12}H_{14}O_2$ requires *M*, 190.0992).

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