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Phenolic Oxidations of Totarol

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Abstract

Methods for the direct oxidation of the C12 position of totarol (1) or its methyl ether (4) have been examined. Treatment of (1) with benzeneseleninic anhydride gave the 9-hydroxy dienone (16) which on ozonolysis afforded the spiro butenolide (21), formed via the ozonide (22). The rearranged ether (18) was obtained from one oxidation with benzeneseleninic anhydride. Mercuriation of totarol and totaryl methyl ether gave the mercuriochlorides (5) and (7) but attempts to form the methoxy acetate (6) from (7) by boronation/oxidation and acetylation were unsuccessful. Treatment of totaryl methyl ether (4) with thallium(III) trifluoroacetate gave dienone 14- and 9-trifluoroacetates (25) and (17). Reaction of the (η^6-arene)tricarbonylchromium(0) complexes (28) and (29) of (4) with lithioacetonitrile gave the 7α-alcohol (30) but reaction with t-butyllithium and then with copper(I) bromide/dimethyl sulfide and Mo**OPH** gave the methoxyphenol (12) in 66% yield.

Introduction

In previous papers[1,2] we reported an investigation of methods for the conversion of totarol (1) into 12-hydroxytotarol (2) with a view to examining oxidative cleavage of the product. Various methods were reported, culminating in cleavage of the aromatic ring of 12,13-dimethoxytotara-8,11,13-triene (3) by ozonolysis to yield (90–95%) the diester (15) which was subsequently converted by a series of steps into conjugated dienolides which have the B/C ring system of the biologically active nagilactones A and C.[3,4] In the earlier work[1] we reported briefly that attempts to oxidize totarol directly with peracids gave no appreciable amounts of oxidized products. We now report the results from a more comprehensive investigation of alternative methods for the introduction of an oxygen function into the 12-position of totarol or its methyl ether (4) as a prelude to oxidative cleavage of the aromatic ring.

[1] Cambie, R. C., Hayward, R. C., and Palmer, B. D., *Aust. J. Chem.*, 1982, **35**, 1679.
[2] Cambie, R. C., Clark, G. R., Rickard, C. E. F., Rutledge, P. S., Ryan, G. R., and Woodgate, P. D., *Aust. J. Chem.*, 1988, **41**, 1171.
[3] Ito, S., and Kodama, M., *Heterocycles*, 1976, **4**, 595.
[4] Hayashi, Y., Matsumoto, T., Uemura, M., and Koreeda, M., *Org. Magn. Reson.*, 1980, **14**, 86.

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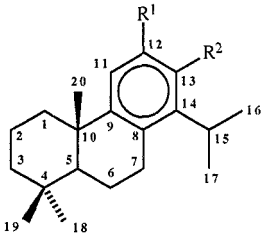
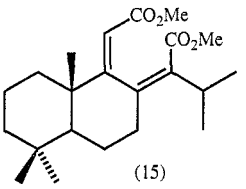


	R^1	R^2		R^1	R^2
(1)	H	OH	(8)	Ac	OH
(2)	OH	OH	(9)	Ac	OMe
(3)	OMe	OMe	(10)	COCH=CH(OH)Me	OMe
(4)	H	OMe	(11)	NO_2	OH
(5)	HgCl	OH	(12)	OH	OMe
(6)	OAc	OMe	(13)	Br	OH
(7)	HgCl	OMe	(14)	Br	OMe



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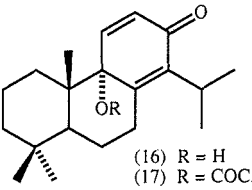
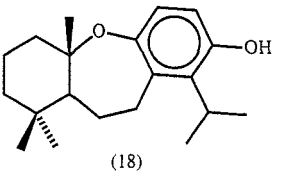


(16) R = H
(17) R = $COCF_3$



(18)

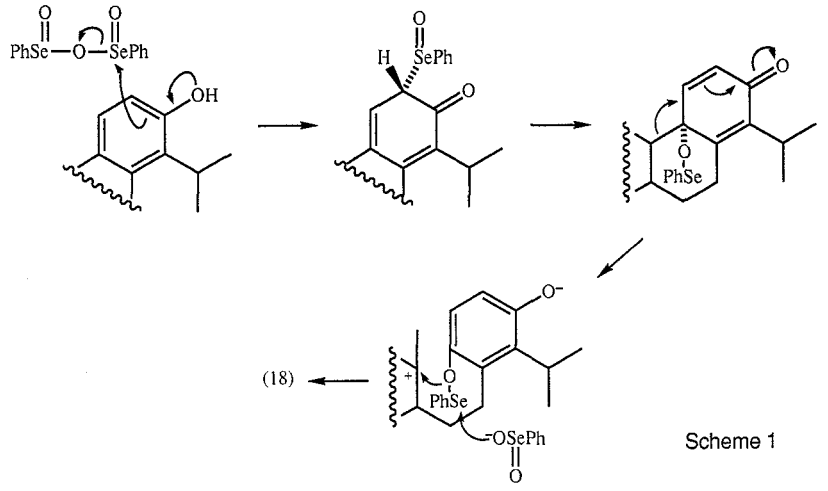
Discussion

Initial attempts to effect selective *ortho*-hydroxylation of totarol were carried out with benzeneseleninic anhydride, a reagent which favours *ortho* oxidation but which is not always selective.[5] In the present case, the major product (38%) from reaction in tetrahydrofuran was the 9-hydroxy dienone (16) which presumably arises from the phenol by *ortho C*-selenenylation followed by a [2,3]-sigmatropic rearrangement,[6] and then nucleophilic cleavage by $PhSeO_2^-$. Models indicate that attack by the reagent at the *ortho*-position of totarol from below the plane of the aryl ring would be the least hindered. The subsequent rearrangement to the *para*-position would then involve α-attack leading to the 9α-hydroxy dienone (16). Repetition of the reaction in acetic anhydride[7] also afforded the 9-hydroxy dienone (16) (30%) although in this case traces of yellow and orange products, possibly 4-hydroxy dienones, were obtained. Attempts to induce formation of an *ortho*-quinone in 1,2-dimethoxyethane at reflux temperature or by generating a phenoxide ion prior to reaction were unsuccessful.

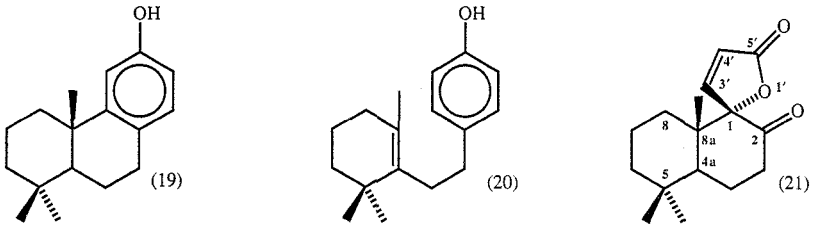
From one experiment another product was isolated for which the structure (18) is suggested. Although the mass spectrum of the compound showed a molecular ion at *m/z* 302 corresponding to the addition of an oxygen atom to totarol, the product was not the desired catechol (2). Thus, while the i.r. spectrum showed a hydroxyl stretching vibration and displayed no carbonyl absorption, and while the ^1H n.m.r. and ^{13}C n.m.r. spectra were remarkably similar to those of totarol, the ^1H n.m.r. spectrum still showed an AB quartet for two vicinal aromatic protons. However, the quartet was centred at δ 6·38, upfield from that observed for totarol (6·75), and the C4 *gem*-dimethyl signals were shifted slightly downfield from those in the spectrum of totarol. The only

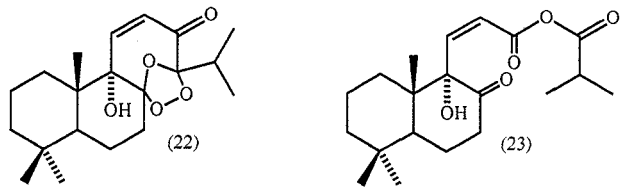
[5] Sukumaran, K. B., and Harvey, R. G., *J. Org. Chem.*, 1980, **45**, 4407.
[6] Barton, D. H. R., Brewster, A. G., Ley, S. V., Read, C. M., and Rosenfeld, M. W., *J. Chem. Soc., Perkin Trans. 1*, 1981, 1473.
[7] Barton, D. H. R., Finet, J.-P., and Thomas, M., *Tetrahedron*, 1988, **44**, 6397.

major differences between the two ^{13}C n.m.r. spectra were the presence of a singlet at δ 81·0 in the SFORD spectrum of (18) indicative of a quaternary carbon bonded to an oxygen atom, and a marked downfield shift of the signal of the aryl carbon corresponding to C9. These data suggest (18) as the probable structure of the product, which can be envisaged as arising from the same intermediate which leads to the 9-hydroxy dienone (16) (Scheme 1). A related mechanism for cleavage of a C9–C10 bond was proposed for the conversion of podocarpa-8,11,13-trien-12-ol (19) into the alkene (20) with hydrogen iodide in acetic acid.[8]



Scheme 1



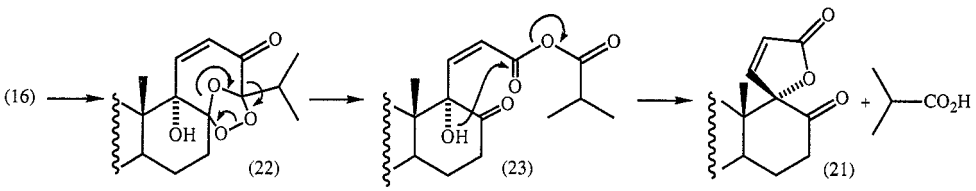


Oxidation of the 9-hydroxy dienone (16) with an excess of ozone in chloroform/methanol (1 : 1) followed by reductive workup afforded a moderate yield (41%) of the spiro γ-lactone (21), the stereochemistry about the spiro carbon atom of which followed from that of the hydroxy group in the starting material.

[8] Cambie, R. C., Davis, B. R., Hayward, R. C., and Woodgate, P. D., *Aust. J. Chem.*, 1975, **28**, 631.

Formation of the lactone (21) can be rationalized (Scheme 2) as involving initial attack of ozone at the more substituted double bond of the dienone (16), followed by rearrangement of the ozonide (22) to give the anhydride (23). Nucleophilic attack at the C13 carbonyl group by the 9α-hydroxy group would then afford the final product. Anomalous ozonolysis products arising from α,β-unsaturated carbonyl compounds through rearrangements of an ozonide are well documented.[9]

When ozonolysis of the dienone (16) was carried out in ethyl acetate without reductive workup the ozonide (22) was obtained as an unstable crystalline product. A single set of signals in the ^{13}C n.m.r. spectrum of (22) in (D_6)benzene showed that only a single ozonide was formed. The ozonide was converted into the spiro lactone (21) upon exposure to acid, e.g. silica (p.l.c.) or chloroform. Signals at δ 18·8 (2), 34·1 and 184·0 in the ^{13}C n.m.r. spectrum of the mixture resulting from acid treatment corresponded with those of isobutyric acid,[10] thereby supporting Scheme 2.



Scheme 2

With the aim of effecting regioselective mercuriation and subsequent replacement of the mercury function by a phenolic group, totarol was treated with mercury(II) acetate in acetonitrile followed by aqueous sodium chloride[11,12] to afford a quantitative yield of 12-chloromercuriototara-8,11,13-trien-13-ol (5). However, attempts to methylate (5) under a variety of conditions led to low yields of (7) and the formation of totarol, while attempts to replace the mercury substituent with trifluoroacetate[13,14] yielded a complex mixture. Attempts to alkylate compound (5) with methyl acrylate and rhodium(III) chloride hydrate[15,16] resulted in isolation of starting material (34%) and totarol (60%) which presumably arose from reaction of (5) with hydrogen chloride generated from the catalyst. Replacement of the rhodium catalyst with palladium(II) acetate led to a mixture of products from which only the dimer podototarin (24)[17] was isolated. Attempted methylation of (5) prior to reaction with diborane/dimethyl

[9] Bailey, P. S., 'Ozonation in Organic Chemistry, Vol. 1. Olefinic Compounds' (Academic Press: London, New York, 1978).

[10] Breitmaier, E., and Voelter, W., 'Carbon-13 NMR Spectroscopy' 3rd Edn (VCH Publishers: Weinheim 1987).

[11] Santaniello, E. and Ferraboschi, P., *J. Chem. Soc., Chem. Commun.*, 1981, 217; Santaniello, E., Fiecchi, A., and Ferraboschi, P., *J. Chem. Soc., Chem. Commun.*, 1982, 1157.

[12] Santaniello, E., Fiecchi, A., Ferraboschi, P., and Ravasi, M., *J. Chem. Soc., Perkin Trans. 1*, 1983, 2765.

[13] Kirk, D. N., and Slade, C. J., *J. Chem. Soc., Chem. Commun.*, 1982, 563.

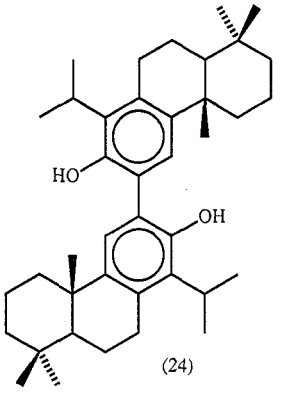
[14] Kalman, J. R., Pinhey, J. T., and Sternhell, S., *Tetrahedron Lett.*, 1972, 5369.

[15] Larock, R. C., 'Organomercury Compounds in Organic Synthesis' Ch. 7, p. 263 (Springer-Verlag: Berlin, New York, 1985).

[16] Heck, R. F., *J. Am. Chem. Soc.*, 1968, **90**, 5518.

[17] Cambie, R. C., Simpson, R., and Colebrook, L. D., *Tetrahedron*, 1963, **19**, 209.

sulfide with the aim of preparing the methoxy acetate (6) according to the method of Santaniello[12] gave a quantitative yield of totarol. Attempted boron exchange of 12-chloromercurio-13-methoxytotara-8,11,13-triene (7), prepared (63%) from (4) with an excess of mercury(II) acetate, returned totaryl methyl ether (100%).



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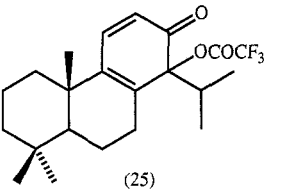

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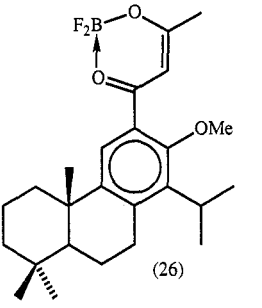


(26)

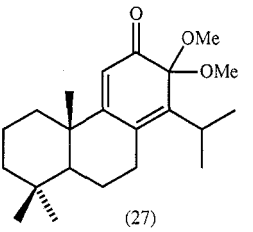
In an attempt to prepare thallium analogues of (5) and (7), totarol and its methyl ether (4) were treated with thallium(III) trifluoroacetate in dry acetonitrile.[18,19] Although (4) returned only starting material, totarol afforded a mixture of products from which the dienone 9α-trifluoroacetate (17) and the dienone 14-trifluoroacetate (25) were isolated in yields of 45 and 12% respectively. The 9-trifluoroacetate was obtained as a single epimer which is assumed to have C 9α stereochemistry by analogy with that of the 9α-hydroxy dienone (16). The u.v. spectra of both (16) and (17) exhibited maxima at *c.* 279 nm. In contrast, the 14-trifluoroacetate (25) was obtained as a mixture of C 14 epimers, the u.v. spectrum of which exhibited a maximum at *c.* 311 nm.[20] Both (17) and (25) were unstable, giving complex mixtures on standing.

Treatment of 13-methoxytotara-8,11,13-triene (4) with boron trifluoride etherate (2 equiv.) in acetic anhydride[12] afforded 12-acetyltotara-8,11,13-trien-13-ol (8), 12-acetyl-13-methoxytotara-8,11,13-triene (9), and the boron difluoride chelate (26), in addition to starting material. In a variation of this experiment, treatment of (4) with boron trifluoride etherate (5 equiv.) in acetic anhydride gave only (8) and (26) in a ratio of 2 : 1. ^{1}H n.m.r. analysis of the crude product showed that the ratio before chromatographic workup was reversed in favour of the chelate. Attempted oxidation of the chelate (26) by treatment with 30% hydrogen peroxide in methanol for 22 h did not effect a Baeyer–Villiger type reaction but resulted only in hydrolysis to afford the enol form (10) of 12-acetoacetyl-13-methoxytotara-8,11,13-triene.

Other oxidations of totarol (1), totara-8,11,13-triene-12,13-diol (2), or the ether (4) were unsuccessful. Thus, treatment of totarol with periodic acid

[18] McKillop, A., Fowler, J. S., Zelesko, M. J., Hunt, J. D., Taylor, E. C., and McGillivray, G., *Tetrahedron Lett.*, 1969, 2433.
[19] Taylor, E. C., Altland, H. W., Danforth, R. H., McGillivray, G., and McKillop, A., *J. Am. Chem. Soc.*, 1970, **92**, 3520.
[20] Burnell, R. H., Jean, M., and Poirier, D., *Can. J. Chem.*, 1987, **65**, 775.

(1 · 1 equiv.) in methanol at room temperature,[21] with benzoyl peroxide in refluxing dichloromethane,[22] or with *m*-chloroperbenzoic acid[23] gave complex mixtures of unidentified products. Attempted reaction of totarol with Fremys salt[24] in methanol or acetone returned starting material while an Elbs persulfate oxidation[25] gave podototarin (24) (68%). Reaction of totarol with copper(II) nitrate (1 equiv.) in acetonitrile[26] resulted in formation of 12-nitrototarol (11) (*c.* 50%) as the only identified product. The nitrophenol (11) was also the only product isolated from treatment of totarol with cerium(IV) ammonium nitrate and hydrogen peroxide.[27] In earlier work we reported[1] that ozonolysis of totarol resulted in extensive degradation. An attempt during the present work to ozonize the dihydric phenol (2), formed (85%) by demethylation of the methoxyphenol (12) with chlorotrimethylsilane and sodium iodide in refluxing acetonitrile,[28] also gave a complex mixture as did treatment of (2) with cerium(IV) ammonium nitrate on silica.[29] Treatment of (12) with periodic acid in methanol[21,30] also gave a complex mixture while treatment with copper(II) chloride in a mixture of anhydrous methanol and anhydrous pyridine in the presence of oxygen[31,32] gave only starting material. However, treatment of (12) with 2,3-dichloro-5,6-dicyanobenzoquinone (1 equiv.) in anhydrous methanol under argon at ambient temperature[33] gave the dimethyl acetal (27) (68%).

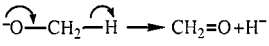


(27)

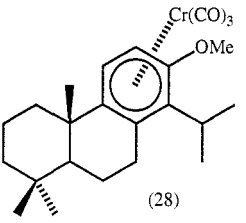
An attempt to replace bromide in compounds (13) or (14) with methoxide in the presence of copper(II) was also unsuccessful. Thus, application of the procedure of Torii *et al.*,[34] using barium oxide, copper(II) chloride and dimethylformamide, to either 12-bromototara-8,11,13-trien-13-ol (13) or 12-bromo-13-methoxytotara-8,11,13-triene (14) returned starting materials as the only identifiable products.

[21] Becker, H.-D., and Gustafsson, K., *J. Org. Chem.*, 1979, **44**, 428.
[22] Matsumoto, T., Ohsuga, Y., Harada, S., and Fukui, K., *Bull. Chem. Soc. Jpn*, 1977, **50**, 266.
[23] Asakawa, Y., Matsuda, R., Tori, M., and Sono, M., *J. Org. Chem.*, 1988, **53**, 5453.
[24] Zimmer, H., Lankin, D. C., and Horgan, S. W., *Chem. Rev.*, 1971, **71**, 229.
[25] Haines, A. H., 'Methods for the Oxidation of Organic Compounds. Alkanes, Alkenes, Alkynes, and Arenes' p. 180 (Academic Press: London 1985).
[26] Afanas'ev, I. B., Gur'yanova, L. F., Baranova, N. G., and Samokhvalov, G. I., *J. Org. Chem. USSR*, 1978, **44**, 527.
[27] Chawla, H. H., Sharma, S. K., Chakrabarty, and Bhanumati, S., *Tetrahedron*, 1988, **44**, 1227.
[28] Olah, G. A., and Narang, S. C., *Tetrahedron*, 1982, **38**, 2225.
[29] Fischer, A., and Henderson, G. N., *Synthesis*, 1985, 641.
[30] Adler, E., and Magnusson, R., *Acta Chem. Scand.*, 1959, **13**, 505.
[31] Barton, D. H. R., Berge-Lurion, R.-M., Lusinchi, X., and Pinto, B. M., *J. Chem. Soc., Perkin Trans. 1*, 1984, 2077.
[32] Hewitt, D. G., *J. Chem. Soc. C*, 1971, 2967.
[33] Arzeno, H., Barton, D. H. R., Berge-Lurion, R.-M., Lusinchi, X., and Pinto, B. M., *J. Chem. Soc., Perkin Trans. 1*, 1984, 2069.
[34] Torri, S., Tanaka, H., Siroi, T., and Akada, M., *J. Org. Chem.*, 1979, **44**, 3305.

Treatment of the bromo ether (14) with sodium methoxide in the presence of copper(I) iodide[35–38] dry methanol, and 2,4,6-collidine gave the ether (4) in quantitative yield. Reductive dehalogenation under these reaction conditions is known and is expected under heterogeneous conditions[35] and/or when the aryl halide bears an *o*-methoxy substituent.[36] Hydride could arise from methoxide



or possibly from methanol. Bacon and coworkers[35] suggest that copper may help to remove the halogen or may provide a temporary site for hydride as a very short lived Cu–H species. A radical pathway is also possible. Treatment of (4) with 30% hydrogen peroxide in the presence of aluminium trichloride[25,30,39] gave a complex mixture.



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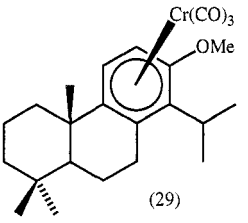


(29)

Table 1. ^{1}H n.m.r. analysis of (28) and (29)

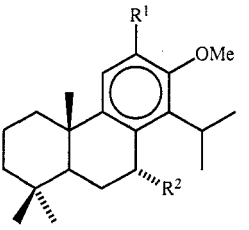
$\delta_H(C_6H_6)$ in $C_6D_6 = 7{\cdot}15$. $\delta_H(C_6H_6)$ in $CDCl_3 = 7{\cdot}35$. $\delta_H[(\eta^6\text{-}C_6H_6)Cr(CO)_3]$ in $C_6D_6 = 4{\cdot}30$. $\delta_H[(\eta^6\text{-}C_6H_6)(Cr(CO)_3]$ in $CDCl_3 = 5{\cdot}33$

Solvent	Proton	Free ligand		α-Complex (28)			β-Complex (29)		
		δ	$\Delta\delta^A$	δ	$\Delta\delta^B$	$\sigma\delta^C$	δ	$\Delta\delta^B$	$\sigma\delta^C$
$CDCl_3$	H11	7·15	−0·2	5·65	0·32	0·52	5·72	0·39	0·59
	H12	6·76	−0·59	4·81	−0·52	0·07	4·90	−0·43	0·16
C_6D_6	H11	7·18	0·03	5·19	0·89	0·86	5·26	0·96	0·93
	H12	6·67	−0·48	4·02	−0·28	0·20	4·16	−0·14	0·34

[A] $\Delta\delta_{Hx} = \delta_{Hx}$(diterpenoid arene) $- \delta_H(C_6H_6)$.
[B] $\Delta\delta_{Hx} = \delta_{Hx}$(diterpenoid complex) $- \delta_H[(\eta^6\text{-}C_6H_6)Cr(CO)_3]$.
[C] $\sigma\delta_{Hx} = \delta_{Hx}$(diterpenoid complex) $- \delta_{Hx}$(diterpenoid arene).

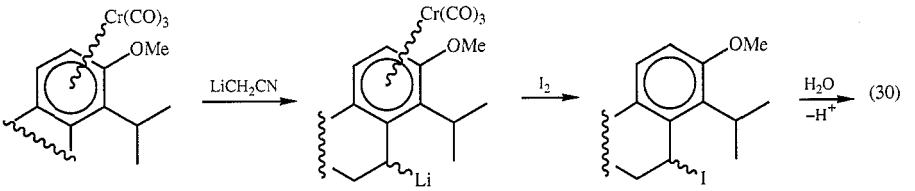
In a further approach, 12-methoxytotara-8,11,13-triene (4) was converted into a mixture (57 : 43) of the stereoisomeric (η^6-arene)tricarbonylchromium(0) complexes (28) and (29) in 51% yield by heating with hexacarbonylchromium(0) in refluxing dibutyl ether/tetrahydrofuran (10 : 3) for 44 h. Analysis of the ^{1}H n.m.r. spectra[40,41] suggested that both complexes adopt a conformation in which

[35] Bacon, R. G. R., and Rennison, S. C., *J. Chem. Soc. C*, 1969, 312.
[36] Lindley, J. *Tetrahedron*, 1984, **40**, 1433.
[37] Cohen, T., *Tetrahedron Lett.*, 1974, 3555.
[38] Cohen, T., and Tirpak, J. G., *Tetrahedron Lett.*, 1975, 143.
[39] Kurz, M. E., and Johnson, G. J., *J. Org. Chem.*, 1971, **36**, 3184.
[40] Cambie, R. C., Clark, G. R., Gourdie, A. C., Rutledge, P. S., and Woodgate, P. D., *J. Organomet. Chem.*, 1985, **297**, 177.
[41] Mailvaganam, B., Perrier, R. E., Sayer, B. G., McCarry, B. E., Bell, R. A., and McGlinchey, M. J., *J. Organomet. Chem.*, 1988, **354**, 325.



	R^1	R^2
(30)	H	OH
(31)	I	H

C 8, C 11 and C 13 are eclipsed (Table 1). With the aim, therefore, of effecting nucleophilic substitution on the aryl ring at C 11, tricarbonyl[(8,9,11,12,13,14-η)-13-methoxytotara-8,11,13-triene]chromium(0) was treated with lithioacetonitrile at −78° followed by oxidative decomplexation with iodine. However, this sequence afforded a mixture from which 13-methoxytotara-8,11,13-triene (4) (15%) and 13-methoxytotara-8,11,13-trien-7α-ol (30) (15%) were the only products identified. The 7α-alcohol (30) probably arises by substitution at C 7 through benzylic lithiation (Scheme 3).[42] The configuration at C 7 was assigned from the H 7 signal, in the ^{1}H n.m.r. spectrum, which appeared as a triplet at δ 5·14 which is consistent with a β-proton. A 7α-proton would exhibit axial–axial coupling with H 6β, axial–equatorial coupling with H 6α, and a 1,3-diaxial coupling with H 5α and thus would be expected to lead to a more complex signal. No trace of the iodide (31), a possible product in Scheme 3, was obtained. An authentic sample of (31) was prepared from (4) by the method of Barluenga *et al.*[43]



Scheme 3

Treatment of the complex (28) and (29) in tetrahydrofuran/*N,N,N′,N′*-tetramethylethylenediamine with butyllithium (4 equiv.) at −78° and then with (hexamethylphosphoric triamide)oxodiperoxy(pyridine)molybdenum (Mo**OPH**)[44] (10 equiv.) followed by reductive workup gave 13-methoxytotara-8,11,13-trien-12-ol (12) in 18% yield. Replacement of the butyllithium by lithium diisopropylamide[45] in an attempt to increase the yield of (12) afforded only starting complex (28) and (29) and the ether (4) (43%). However, treatment of the complex (28) and (29) with t-butyllithium (5 equiv.) and then Mo**OPH** (10 equiv.) gave the methoxy phenol (12) in 25% yield. Moreover, when the complex was

[42] Brocard, J., and Lebibi, J., *J. Organomet. Chem.*, 1987, **320**, 295.
[43] Barluenga, J., Campos, P., Gonzalez, J., and Asensio, G., *J. Chem. Soc., Perkin Trans. 1*, 1984, 2623.
[44] Gill, J. C., Marples, B. A., and Traynor, J. R., *Tetrahedron Lett.*, 1987, **28**, 2643.
[45] Fraser, R. R., and Mansour, T. S., *J. Organomet. Chem.*, 1986, **310**, C60.

treated with t-butyllithium (5 equiv.) and copper(I) bromide/dimethyl sulfide complex[46] and then with Mo**OPH** (10 equiv.) at −78° the methoxy phenol (12) was obtained in 66% yield.

Experimental

For general experimental details see refs 1, 47 and 48.

Oxidation of Totarol (1) with Benzeneseleninic Anhydride

(A) A solution of totarol (1·53 g) in dry tetrahydrofuran (20 ml) was added dropwise over 40 min to a suspension of benzeneseleninic anhydride (1·94 g) in dry tetrahydrofuran (50 ml) at 55°, and the temperature was maintained between 48° and 58° until no starting material remained (45 min, t.l.c.). The mixture was diluted with chloroform (100 ml) and washed with sodium hydrogencarbonate and water, and dried. Removal of solvent under vacuum gave an oil which was chromatographed on silica. Elution with hexane/ether (4 : 1) gave diphenyl diselenide, a large brown band containing unidentified products, and then *9α-hydroxytotara-8(14),11-dien-13-one* (16) (0·60 g), 38%) which crystallized from ether/hexane as needles, m.p. 179–181° (sealed tube), $[\alpha]_D^{15}$ +24° (*c*, 0·2) (Found: C, 79·1; H, 10·3. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·0%), λ_{max} 244 (ϵ 7070), 280sh nm (3730). ν_{max} 3575–3150 (OH), 1660 (CO), 1625 cm^{-1} (C=C). δ_H 0·73, s, $(H20)_3$; 0·82, s, $(H19)_3$; 0·95, s, $(H18)_3$; 1·20, 1·21, 2d, $J_{16,15} = J_{17,15}$ 7·1 Hz, $(H16)_3$, $(H17)_3$; 1·27, ddd, $J_{3\alpha,3\beta}$ 13·1, $J_{3\alpha,2\beta}$ 13·1, $J_{3\alpha,2\alpha}$ 4·7 Hz, H3α; 1·37, m, H3β; 1·37, m, H1β; 1·39, dddd, $J_{6\beta,6\alpha}$ 13·1, $J_{6\beta,7\alpha}$ 13·3, $J_{6\beta,5\alpha}$ 12·9, $J_{6\beta,7\beta}$ 4·2 Hz, H6β; 1·53, m, H2α; 1·57, ddddd, $J_{2\beta,2\alpha}$ 13·2, $J_{2\beta,1\alpha}$ 13·1, $J_{2\beta,3\alpha}$ 13·1, $J_{2\beta,1\beta}$ 3·4, $J_{2\beta,3\beta}$ 3·4 Hz, H2β; 1·86, dddd, $J_{6\alpha,6\beta}$ 13·1, $J_{6\alpha,7\alpha}$ 5·5, $J_{6\alpha,7\beta}$ 3·2, $J_{6\alpha,5\alpha}$ 3·2 Hz, H6α; 1·93, ddd, $J_{1\alpha,1\beta}$ 12·5, $J_{1\alpha,2\beta}$ 13·1, $J_{1\alpha,2\alpha}$ 5·3 Hz, H1α; 2·04, dd, $J_{5\alpha,6\beta}$ 12·9, $J_{5\alpha,6\alpha}$ 3·2 Hz, H5; 2·51, ddd, $J_{7\alpha,7\beta}$ 13·3, $J_{7\alpha,6\beta}$ 13·3, $J_{7\alpha,6\alpha}$ 5·5 Hz, H7α; 2·90, ddd, $J_{7\beta,7\alpha}$ 13·3, $J_{7\beta,6\beta}$ 4·2, $J_{7\beta,6\alpha}$ 3·2 Hz, H7β; 3·24, sept., $J_{15,16} = J_{15,17}$ 7·1 Hz, H15; 6·17, d, $J_{12,11}$ 10·1 Hz, H12; 6·81, d, $J_{11,12}$ 10·1 Hz, H11. δ_C 15·4, C19; 18·95, C2; 20·76, 21·31, C16, C17; 21·67, C20; 23·60, C6; 26·09, C15; 27·02, C7; 33·05, C1; 33·62, C4; 33·66, C18; 41·51, C3; 44·16, C5; 45·72, C10; 74·92, C9; 130·25, C12; 138·58, C14; 147·32, C11; 157·06, C8; 185·67, C13. *m/z* 302 (M, 83%), 287 (1), 220 (66), 165 (100), 164 (72), 137 (92), 81 (56), 69 (71), 55 (66), 43 (38), 41 (86).

Attempted reaction at room temperature for 14·5 h gave starting material.

(B) A solution of totarol (0·15 g) and benzeneseleninic anhydride (0·20 g) in dry tetrahydrofuran (13 ml) was stirred at 48–63° for 75 min, and the mixture was diluted with chloroform (30 ml), and worked up as in (A) to give an oil which was chromatographed (p.l.c.) on silica. Elution with dichloromethane/hexane (2 : 1) gave a large number of bands. A band, R_F 0·11, gave an oil which was purified by multiple p.l.c. (hexane/ether, 17 : 3) to give a major band, R_F 0·3, which afforded a white solid. Crystallization from hexane/ether (99 : 1) gave the ether (18) (25 mg, 15%) as needles, m.p. 90°. An elemental analysis was not obtained. λ_{max} ($CHCl_3$) 238, 286 nm. ν_{max} 3600–3200 (OH), 1095 (C–O), 660 cm^{-1} (OH). δ_H 0·83, 0·88, 2s, $(H18)_3$, $(H19)_3$; 1·20, s, $(H20)_3$; 1·36, d, *J* 7 Hz, $(H16)_3$, $(H17)_3$; 3·43, sept., *J* 7 Hz, H15; 4·64, br s, OH; 6·28, 6·48, AB q, aryl H. δ_C 150·18, s; 148·36, s; 135.02, s; 131·77, s; 120·35, d; 113·17, d; 81·32, s; 52·95, d; 41·59, t; 40·68, t; 34·71, s; 32·72, q; 27·50, d; 26·46, t; 21·59; 21·52; 21·43; 21·07, 2C, q, C16, C17; 20·71, t. *m/z* 302 (M, 100%), 231 (16), 205 (34), 165 (65), 137 (93), 123 (32), 95 (36), 81 (36), 69 (25), 55 (37), 43 (32), 41 (47).

Ozonolysis of the 9-Hydroxy Dienone (16)

(A) A cooled (−78°) solution of the 9-hydroxy dienone (16) (0·11 g) in chloroform/methanol (1 : 1, 25 ml) was treated with a stream of ozonized oxygen until a blue colour developed.

[46] Beswick, P. J., Leach, S. J., Masters, N. F., and Widdowson, D. A., *J. Chem. Soc., Chem. Commun.*, 1984, 46.

[47] Cambie, R. C., Pang, G. T. M., Parnell, J. C., Rodrigo, R., and Weston, R. J., *Aust. J. Chem.*, 1979, **32**, 2741.

[48] Cambie, R. C., Coddington, J. M., Rutledge, P. S., Taylor, C. M., and Woodgate, P. D., *Aust. J. Chem.*, 1989, **42**, 1115.

Excess of ozone was removed in a stream of argon as the solution was warmed to room temperature. Dimethyl sulfide (1 mol equiv.) was added and solvents were removed under vacuum to give an oil which was chromatographed (p.l.c.) on silica. Elution with hexane/ether (1 : 1) gave a band, R_F 0·55, which was extracted into dichloromethane. Removal of the solvent under vacuum gave *5,5,8a-trimethyloctahydronaphthalene-1(2H)-spiro-2′(5′H)-furan-2,5′-dione* (21) (40 mg, 41%) which, after Kugelrohr distillation at 90°/0.05 mm, crystallized as needles, m.p. 85–86° (Found: C, 73·4; H, 8·5%; $M^{+\bullet}$, 262·1579. $C_{16}H_{22}O_3$ requires C, 73·3; H, 8·5%; $M^{+\bullet}$, 262·1569). ν_{max} 1760 (γ-lactone), 1720 (CO), 1603 (C=C), 1127, 1090 cm^{-1} (C–O). δ_H 0·90, s, 5β-Me; 0·98, s, 5α-Me; 0·99, dm, $J_{8\beta,8\alpha}$ 13·1 Hz, H8β; 1·10, s, 8a-Me; 1·25, ddd, $J_{6\alpha,6\beta}$ 13·3, $J_{6\alpha,7\beta}$ 13·3, $J_{6\alpha,7\alpha}$ 4·3 Hz, H6α; 1·35, ddd, $J_{8\alpha,8\beta}$ 13·1, $J_{8\alpha,7\beta}$ 13·1, $J_{8\alpha,8\alpha}$ 4·4 Hz, H8α; 1·42, dm, $J_{6\beta,6\alpha}$ 13·3 Hz, H6β; 1·50, m, H7α; 1·56, ddddd, $J_{7\beta,7\alpha}$ 13·6, $J_{7\beta,6\alpha}$ 13·3, $J_{7\beta,8\alpha}$ 13·1, $J_{7\beta,6\beta}$ 3·3, $J_{7\beta,8\beta}$ 3·3 Hz, H7β; 1·73, dddd, $J_{4\beta,4\alpha}$ 13·7, $J_{4\beta,3\alpha}$ 13·7, $J_{4\beta,3\beta}$ 4·8 Hz, H4β; 2·08, m, H4a; 2·09, m, H4α; 2·47, ddd, $J_{3\beta,3\alpha}$ 13·7, $J_{3\beta,4\beta}$ 4·8, $J_{3\beta,4\alpha}$ 2·0 Hz, H3β; 2·92, ddd, $J_{3\alpha,3\beta}$ 13·7, $J_{3\alpha,4\beta}$ 13·7, $J_{3\alpha,4\alpha}$ 7·1 Hz, H3α; 6·13, d, $J_{4',3'}$ 6·0 Hz, H4′; 7·59, d, $J_{3',4'}$ 6·0 Hz, H3′. δ_C 16·3, 8a-Me; 17·95, C7; 21·80, 5β-Me; 23·15, C4; 31·73, C8; 33·12, C 5α-Me; 33·76, C5; 39·52, C3; 40·96, C6; 45·17, C8a; 45·62, C4a; 97·19, C1; 122·44, C4′; 155·04, C3′; 170·97, C2; 205·72, C5′. *m/z* 262 (M, 24%), 244 (32), 137 (95), 123 (34), 109 (31), 95 (50), 81 (47), 69 (100), 55 (74), 41 (93).

(B) A stream of ozonized oxygen was bubbled through a solution of the dienone (16) (0·11 g, 0·35 mmol) in ethyl acetate (20 ml) at −78° until the solution became blue. Excess of ozone was removed in a stream of nitrogen and solvents were removed under reduced pressure to give the unstable ozonide (22) (100%) which crystallized from hexane/ether as needles, m.p. 77–79°. δ_H (C_6D_6) 0·74, s, $(H20)_3$; 0·80, s, $(H19)_3$; 0·99, s, $(H18)_3$; 1·00, 1·01, 2d, $J_{16,15} = J_{17,15}$ 6·8 Hz, $(H16)_3$, $(H17)_3$; 1·71, dd, *J* 8·9, 6·4 Hz; 1·88, ddd, *J* 14·1, 3·2, 3·2 Hz; 1·95, ddd, *J* 13·0, 13·0, 4·3 Hz; 2·14, ddd, *J* 14·1, 11·1, 8·4 Hz; 3·20, sept., $J_{15,16} = J_{15,17}$ 6·8 Hz, H15; 5·61, d, $J_{12,11}$ 9·9 Hz, H12; 6·27, d, $J_{11,12}$ 9·9 Hz, H11. δ_C (C_6D_6) 17·05, C20; 18·01, 18·32, C16, C17; 18·38, C2; 19·74, C6; 22·03, C19; 29·45, C7; 31·62, C1; 33·12, C4; 33·63, C18; 36·17, C15; 41·59, C3; 41·88, C10; 43·65, C5; 77·38, C9; 103·39, C14; 112·22, C8; 125·01, C12; 133·82, C11; 202·94, C13.

Mercuriation of Totarol (1)

Mercury(II) acetate (0·11 g, 0·35 mmol) was added to a stirred solution of totarol (0·10 g, 0·33 mmol) in dry acetonitrile (3 ml) and the mixture was heated under reflux under nitrogen for 2 h. The mixture was diluted with brine, extracted with dichloromethane, and the extracts were washed with water and dried. Removal of solvent under reduced pressure gave *12-chloromercuriototara-8,11,13-trien-13-ol* (5) (100%) which crystallized from chloroform/hexane as needles, m.p. 168–172° (dec.) (Found: C, 46·4; H, 5·9. $C_{20}H_{29}ClHgO$ requires C, 46·1; H, 5·6%). ν_{max} 3625–3200 (OH), 1440, 1090, 715 cm^{-1}. δ_H 0·92, s, $(H19)_3$; 0·96, s, $(H18)_3$; 1·19, s, $(H20)_3$; 1·19–1·32, m, 2H; 1·26, dd, $J_{5\alpha,6\beta}$ 12·4, $J_{5\alpha,6\alpha}$ 1·3 Hz, H5; 1·35, 1·36, 2d, $J_{16,15} = J_{17,15}$ 7·3 Hz, $(H16)_3$, $(H17)_3$; 1·48, dm, $J_{3\beta,3\alpha}$ 13·1 Hz, H3β; 1·58–1·70, m,, H2α, H6β; 1·73, ddddd, $J_{2\beta,2\alpha}$ 13·8, $J_{2\beta,1\alpha}$ 13·8, $J_{2\beta,1\alpha}$ 13·8, $J_{2\beta,1\beta}$ 3·2, $J_{2\beta,3\beta}$ 3·2 Hz, H2β; 1·93, dd, $J_{6\alpha,6\beta}$ 14·1, $J_{6\alpha,7\alpha}$ 7·9 Hz, H6α; 2·22, dm, $J_{1\beta,1\alpha}$ 12·4 Hz, H1β; 2·79, ddd, $J_{7\alpha,7\beta}$ 17·2, $J_{7\alpha,6\beta}$ 11·1, $J_{7\alpha,6\alpha}$ 8·0 Hz, H7α; 2·96, dd, $J_{7\beta,7\alpha}$ 17·2, $J_{7\beta,6\beta}$ 6·3 Hz, H7β; 3·43, sept., $J_{15,16} = J_{15,17}$ 7·3 Hz, H15; 4·92, s, OH; 7·00, s, H11. δ_C 19·14, C2; 19·40, C6; 20·72, 20·74, C16, C17; 21·52, C19; 25·19, C20; 26·57, C15; 28·73, C7; 33·17, C18; 33·25, C4; 38·03, C10; 39·58, C1; 41·41, C3; 49·43, C5; 130·22, C11; 130·95, C8; 135·21, C14; 136·06, C9; 144·55, C12; 153·48, C13. *m/z* 522 (M, 6·5%), 520 (5), 507 (19), 505 (14), 286 (33), 271 (100), 201 (45), 189 (27), 175 (66), 129 (24), 69 (78), 55 (62), 43 (77), 41 (78).

Attempted oxidation of the organomercurial with lead tetraacetate in trifluoroacetic acid at room temperature under nitrogen for 90 min gave a complex mixture of products. Attempted methylation of the organomercuric phenol with (i) sodium hydride and iodomethane under reflux (90 min) gave the methyl ether (7) (36%) and totarol (60%); (ii) sodium hydride and iodomethane at room temperature (2 h) gave (5) (37%) and totarol (63%); (iii) trimethylsulfonium hydroxide in dimethylformamide under reflux (90 min) gave totarol (100%); and (iv) sodium hydroxide and dimethyl sulfate at room temperature (20 h) and then under reflux (4 h) gave (5) (50%) and totarol (5%).

Mercuriation of 13-Methoxytotara-8,11,13-triene (4)

Mercury(II) acetate (60 mg, 0·18 mmol) was added to a solution of the ether (4) (50 mg, 0·17 mmol) in dry acetonitrile (5 ml) and the solution was heated under reflux for 50 h. Further mercury(II) acetate (60 mg, 0·18 mmol) was added at intervals. Solvent was removed from the cooled mixture under reduced pressure to give a solid which was dissolved in tetrahydrofuran. The solution was filtered, diluted with brine (2 ml), refiltered, and concentrated to give *12-chloromercurio-13-methoxytotara-8,11,13-triene* (7) (57 mg, 63%) which crystallized from dichloromethane/hexane as fine needles, m.p. 287–288° (dec.) (sublimation >230°) (Found: C, 47·2; H, 5·8. $C_{21}H_{31}ClHgO$ requires C, 47·1; H, 5·8%). ν_{max} 1460, 1360, 1230, 1000 cm^{-1}. δ_H 0·92, s, $(H19)_3$; 0·95, s, $(H18)_3$; 1·19, s, $(H20)_3$; 1·20, ddd, $J_{3\alpha,3\beta}$ 13·4, $J_{3\alpha,2\beta}$ 13·4, $J_{3\alpha,2\alpha}$ 4·6 Hz, H3α; 1·26, dd, $J_{5\alpha,6\beta}$ 12·6, $J_{5\alpha,6\alpha}$ 2·4 Hz, H5; 1·31, 1·32, 2d, $J_{16,15} = J_{17,15}$ 7·1 Hz, $(H16)_3$, $(H17)_3$; 1·36, ddd, $J_{1\alpha,1\beta}$ 13·0, $J_{1\alpha,2\beta}$ 13·0, $J_{1\alpha,2\alpha}$ 3·7 Hz, H1α; 1·48, dm, $J_{3\beta,3\alpha}$ 13·4 Hz, H3β; 1·57–1·69, m, H2α, H6β; 1·74, ddddd, $J_{2\beta,2\alpha}$ 13·6, $J_{2\beta,3\alpha}$ 13·4, $J_{2\beta,1\alpha}$ 13·0, $J_{2\beta,1\beta}$ 3·3, $J_{2\beta,3\beta}$ 3·3 Hz, H2β; 1·92, dddd, $J_{6\alpha,6\beta}$ 13·2, $J_{6\alpha,7\alpha}$ 7·8, $J_{6\alpha,5\alpha}$ 2·4, $J_{6\alpha,7\beta}$ 2·4 Hz, H6α; 2·22, dm, $J_{1\beta,1\alpha}$ 13·0 Hz, H1β; 2·82, ddd, $J_{7\alpha,7\beta}$ 17·4, $J_{7\alpha,6\beta}$ 11·0, $J_{7\alpha,6\alpha}$ 7·8 Hz, H7α; 3.00, dd, $J_{7\beta,7\alpha}$ 17·4, $J_{7\beta,6\beta}$ 5·5 Hz, H7β; 3·36, m, H15; 3·85, s, OMe; 7·05, s, H11. δ_C 19·18; 19·38, C2, C6; 21·42, 21·42; 21·55, C16, C17, C19; 24·99, C20; 27·63, C15; 28·59, C7; 33·15, C18; 33·33, C4; 38·34, C10; 39·51, C1; 41·40, C3; 49·42, C5; 62·94, OMe; 130·27, C11. *m/z* 536 (M, 17%), 521 (30), 451 (13), 439 (12), 425 (20), 285 (47), 215 (21), 189 (27), 129 (22), 97 (26), 83 (41), 69 (100).

Attempts to substitute the mercuriochloride with boron by using diborane/tetrahydrofuran/hydrogen peroxide, or diborane/dimethyl sulfide/hydrogen peroxide, gave totaryl methyl ether (100%), while trimethyl borate gave starting material. Attempts to substitute with oxygen by using hydrogen peroxide, *m*-chloroperbenzoic acid, Mo**OPH** or Jones reagent each gave starting material or toraryl methyl ether.

Attempted Alkylations of 12-Chloromercuriotota-8,11,13-trien-13-ol (5)

(A) *With methyl acrylate and rhodium(III) chloride.*—A solution of the organomercuric phenol (5) (35 mg, 0·07 mmol) and $RhCl_3.xH_2O$ (20 mg) in dry acetonitrile (2 ml) was stirred at room temperature under nitrogen for 30 min. Methyl acrylate (50 μl, 0·54 mmol) was added and the mixture was stirred for a further 22 h. The mixture was diluted with water, extracted with dichloromethane, and the extracts were washed with brine and dried. Removal of solvent under reduced pressure gave a yellow oil which was chromatographed (p.l.c.) on silica and eluted with hexane/ether (3 : 1). A band, R_F 0·53, gave starting material (13 mg, 34%) and a band, R_F 0·63, gave totarol (1) (12 mg, 60%) (identical ^1H n.m.r. spectrum).

(B) *With methyl acrylate and palladium(II) acetate.*—Palladium(II) acetate (70 mg, 0·22 mmol) was added to a solution of the organomercuric phenol (5) (0·10 g, 0·2 mmol) and methyl acrylate (125 μl, 1·35 mmol) in dry acetonitrile (6 ml) and the mixture was stirred at room temperature under nitrogen for 45 min. The mixture was diluted with water, extracted with ether, and the aqueous phase was acidified with 2 mol l^{-1} hydrochloric acid and reextracted with ether. The combined extracts were washed with brine and dried and filtered through a pad of Celite. Removal of solvent under reduced pressure gave an orange glass which was chromatographed (p.l.c.) on silica and eluted with hexane/ether (9 : 1). The major band R_F 0·85, afforded podototarin (24) as a glass (6 mg) (correct i.r. and ^1H n.m.r. spectra[17]). *m/z* 570 (M, 6%), 555 (M−Me, 5), 526 (100), 511 (30), 415 (30), 331 (10), 285 (9), 258 (8), 69 (31), 41 (32).

Treatment of Totarol (1) with Thallium(III) Trifluoroacetate

A solution of totarol (0·19 g, 0·65 mmol) and thallium(III) trifluoroacetate (0·36 g, 0·66 mmol) in dry acetonitrile (6 ml) was stirred at room temperature under nitrogen for 2 h. The mixture was diluted with water, extracted with dichloromethane, and the extracts were washed with water and brine, and dried. Removal of solvent under reduced pressure gave an oil which was chromatographed (p.l.c.) on silica and eluted with hexane/ether (12 : 1). A band, R_F 0·5, gave the *13-oxototara-8(14),11-dien-9α-yl trifluoroacetate* (17) (0·12 g, 45%)

as an unstable pale yellow oil (Found: $M^{+\bullet}$, 398·2062. $C_{22}H_{29}F_3O_3$ requires $M^{+\bullet}$, 398·2069). λ_{max} ($CHCl_3$) 279 nm. ν_{max} 1785 ($COCF_3$), 1665 (CO), 1635 (C=C), 1200, 1150–1120 (CF), 845 cm^{-1}. δ_H 0·79, s, $(H20)_3$; 0·84, s, $(H19)_3$; 0·97, s, $(H18)_3$; 1·23, 1·24, 2d, $J_{16,15}$ = $J_{17,15}$ 7·1 Hz, $(H16)_3$, $(H17)_3$; 1·25, ddd, $J_{3\alpha,3\beta}$ 12·8, $J_{3\alpha,2\beta}$ 12·8, $J_{3\alpha,2\alpha}$ 6·7 Hz, H3α; 1·38–1·50, m, 3H; 1·52–1·68, m, H2β, H6β, 1·82–1·94, m, 4H; 2·98–3·06, m, 1H; 3·26, sept., $J_{15,16}$ = $J_{15,17}$ 7·1 Hz, H15; 6·39, d, $J_{12,11}$ 10·2 Hz, H12; 6·65, d, $J_{11,12}$ 10·2 Hz, H11. δ_C 14·36, C20; 18·89, C2; 20·55, 20·99, C16, C17; 21·56, C19; 23·66, C6; 26·49, C15; 27·03, C7; 33·52, C1; 33·82, C4; 33·86, C18; 41·29, C3; 45·32, C5; 47·34, C10; 86·61, C9; 114·2, q, $^1J_{CF}$ 286 Hz, CO**C**F_3; 133·34, C12; 140·26, C11; 141·35, C14; 149·01, C8; 154·69, q, $^2J_{CF}$ 43 Hz, **C**OCF_3; 184·67, C13. *m/z* 398 (M, 11%), 383 (14), 356 (12), 342 (16), 341 (74), 313 (13), 301 (13), 286 (24), 272 (15), 271 (67), 259 (29), 245 (22), 201 (29), 189 (16), 175 (43), 69 (100), 55 (28), 43 (42), 41 (42).

A band, R_F 0·6, gave the *13-oxototara-8(14),11-dien-14-yl trifluoroacetate* (25) (31 mg, 12%) as an unstable yellow oil (Found: $M^{+\bullet}$, 398·2071. $C_{22}H_{29}F_3O_3$ requires $M^{+\bullet}$, 398·2069). λ_{max} ($CHCl_3$) 311 nm. ν_{max} 1790 ($COCF_3$), 1680 (CO), 1630 (C=C), 1460, 1210, 1150 (CF), 750 cm^{-1}. δ_H 0·88, s, $(H19)_3$; 0·93, 1·00, 2d, $J_{16,15}$ = $J_{17,15}$ 7·0 Hz, $(H16)_3$, $(H17)_3$; 0·95, s, $(H18)_3$; 1·05, s, $(H20)_3$; 1·12, dd, $J_{5\alpha,6\beta}$ 12·5, $J_{5\alpha,6\alpha}$ 1·5 Hz, H5; 2·28, sept., $J_{15,16}$ = $J_{15,17}$ 7·0 Hz, H15; 6·10, d, $J_{12,11}$ 10·4 Hz, H12; 7·15, d, $J_{11,12}$ 10·4 Hz, H11. δ_C 15·02, 15·96, C16, C20; 17·92, C2; 18·76, C6; 20·85, 21·44, C17, C19; 26·27, C7; 33·06, C18,; 33·20, C4; 35·79, C15; 36·81, C1; 37·29, C10; 41·18, C3; 51·28, C5; 90·23, C14; 114·37, q, $^1J_{CF}$ 284 Hz, CO**C**F_3; 125·79, C12; 141·11, 141·35, C8, C9; 142·28, C11; 155·46, q, $^2J_{CF}$ 42 Hz, **C**OCF_3; 196·55, C13. *m/z* 398 (M, 12%), 383, (12), 356 (18), 342 (21), 341 (100), 313 (12), 287 (14), 286 (17), 271 (46), 259 (35), 245 (27), 201 (22), 175 (30), 69 (100), 43 (50), 41 (48).

Attempted thallation of the methyl ether (4) with thallium(III) trifluoroacetate in dry acetonitrile at room temperature under nitrogen for 4·5 h gave starting material (100%).

Treatment of 13-Methoxytotara-8,11,13-triene (4) with Boron Trifluoride Etherate

(A) Boron trifluoride etherate (*c.* 45% BF_3, 0·1 ml, 0·7 mmol) was added to a mixture of the ether (4) (0·20 g, 0·67 mmol) in acetic anhydride (10 ml) at 0° and the mixture was stirred at room temperature under nitrogen for 3 h. Additional reagent (0·1 ml) was added and the mixture was stirred for a further 17 h. The mixture was diluted with water, extracted with ether, and the extracts were washed with brine and dried. Removal of the solvents under reduced pressure gave an oil which was chromatographed (p.l.c.) on silica and eluted with hexane/ether (6 : 1). A band, R_F 1·0, gave starting material (79 mg, 40%) while a band, R_F 0·8, gave *12-acetyltotara-8,11,13-trien-13-ol* (8) (47 mg, 21%) which crystallized from hexane as pale yellow hexagonal prisms, m.p. 144–146° (Found: C, 80·2; H, 9·7. $C_{22}H_{32}O_2$ requires C, 80·4; H, 9·8%). ν_{max} 3200–2400 (OH) 1630 (CO), 1610 (C=C), 1450, 1350, 1290, 1105, 800, 590 cm^{-1}. δ_H 0·94, s, $(H19)_3$; 0·97, s, $(H18)_3$; 1·20, s, $(H20)_3$; 1·23, ddd, $J_{3\alpha,3\beta}$ 13·5, $J_{3\alpha,2\beta}$ 13·5, $J_{3\alpha,2\alpha}$ 4·1 Hz, H3α; 1·27, dd, $J_{5\alpha,6\beta}$ 12·6, $J_{5\alpha,6\alpha}$ 2·2 Hz, H5; 1·36, 1·37, 2d, $J_{16,15}$ = $J_{17,15}$ 6·8 Hz, $(H16)_3$, $(H17)_3$; 1·40, ddd, $J_{1\alpha,1\beta}$ 12·9, $J_{1\alpha,2\beta}$ 12·9, $J_{1\alpha,2\alpha}$ 3·7 Hz, H1α; 1·50, dm, $J_{3\beta,3\alpha}$ 13·5 Hz, H3β; 1·61–1·73, m, H2α, H6β; 1·76, ddddd, $J_{2\beta,2\alpha}$ 13·5, $J_{2\beta,3\alpha}$ 13·5, $J_{2\beta,1\alpha}$ 12·9, $J_{2\beta,1\beta}$ 3·3, $J_{2\beta,3\beta}$ 3·3 Hz, H2β; 1·95, dd, $J_{6\alpha,6\beta}$ 13·4, $J_{6\alpha,7\alpha}$ 8·2 Hz, H6α; 2·29, dm, $J_{1\beta,1\alpha}$ 12·9 Hz, H1β; 2·81, ddd, $J_{7\alpha,7\beta}$ 18·1, $J_{7\alpha,6\beta}$ 11·0, $J_{7\alpha,6\alpha}$ 8·2 Hz, H7α; 3·00, dd, $J_{7\beta,7\alpha}$ 18·1, $J_{7\beta,6\beta}$ 6·3 Hz, H7β, 3·28, m, H15; 7·53, s, H11; 11·75, s, OH. δ_C 19·02, 19·35, C2, C6; 19·65, 21·55, C16, C19; 21·55, 25·33, C17, C20; 26·62, CO**Me**; 27·55, C15; 29·17, C7; 33·13, C18; 33·26, C4; 37·56, C10; 39·70, C1; 41·43, C3; 49·25, C5; 112·72, s, aryl C; 124·31, C11; 133·15, s, aryl C; 141·26, s, aryl C; 142·81, s, aryl C; 159·05, s, aryl C; 204·52, **C**OMe. *m/z* 328 (M, 49%), 314 (23), 313 (100), 271 (7), 245 (14), 243 (31), 231 (17), 217 (49), 69 (26), 55 (13), 43 (87), 41 (21). A band, R_F 0.5, gave 12-acetyl-13-methoxytotara-8-11,13-triene (9) (45 mg, 20%) as a crystalline solid,[1] m.p. and mixed m.p. 159° (sublimation). δ_H 0·92, s, $(H19)_3$; 0·95, s, $(H18)_3$; 1·18, s, $(H20)_3$; 1·19, ddd, $J_{3\alpha,3\beta}$ 13·0, $J_{3\alpha,2\beta}$ 13·0, $J_{3\alpha,2\alpha}$ 4·2 Hz, H3α, 1·25, dd, $J_{5\alpha,6\beta}$ 12·7, $J_{5\alpha,6\alpha}$ 2·2 Hz, H5; 1·33, 1·34, 2d, $J_{16,15}$ = $J_{17,15}$ 7·0 Hz, $(H16)_3$, $(H17)_3$; 1·35, ddd, $J_{1\alpha,1\beta}$ 13·2, $J_{1\alpha,2\beta}$ 13·2, $J_{1\alpha,2\alpha}$ 3·7 Hz, H1α; 1·47, dm, $J_{3\alpha,3\alpha}$ 13·0 Hz, H3β; 1·56–1·70, m, H2α, H6β; 1·72, ddddd, $J_{2\beta,2\alpha}$ 13·7, $J_{2\beta,1\alpha}$ 13·2, $J_{2\beta,3\alpha}$ 13·0, $J_{2\beta,1\beta}$ 3·3, $J_{2\beta,3\beta}$ 3·3 Hz, H2β; 1·92, dd, $J_{6\alpha,6\beta}$ 13·3, $J_{6\alpha,7\alpha}$ 8·0 Hz, H6α; 2·28, dm, $J_{1\beta,1\alpha}$ 13·2 Hz,

H1β; 2·60, s, Ac; 2·80, ddd, $J_{7\alpha,7\beta}$ 17·7, $J_{7\alpha,6\beta}$ 10·6, $J_{7\alpha,6\alpha}$ 7·5 Hz, H7α; 2·96, dd, $J_{7\beta,7\alpha}$ 17·7, $J_{7\beta,6\beta}$ 6·3 Hz, H7β; 3·34, m, H15; 3·68, s, OMe; 7·32, s, H11. δ_C 19·10, 19·27, C2, C6; 21·45, C16; 21·45, C17; 21·55, C19; 24·88, C20; 27·44, C15; 28·96, C7; 29·83, CO**Me**; 33·14, C18; 33·28, C4; 38·00, C10; 39·35, C1; 41·41, C3; 49·31, C5; 63·22, OMe; 124·05, C11; 131·78, 138·85, C12, C14; 138·90, C8; 146·27, C9; 156·32, C13; 202·42, **C**OMe. m/z 342 (M, 65%), 328 (20), 327 (100), 285 (10), 259 (24), 257 (41), 245 (37), 232 (11), 231 (64), 69 (30), 55 (16), 43 (66), 41 (23).

A band, R_F 0·3, gave the *boron difluoride chelate* (26) (35 mg, 12%) which crystallized from hexane/ether as needles, m.p. 159–161° (Found: C, 69·7; H, 8·9. $C_{25}H_{35}BF_2O_3$ requires: C, 69·4; H, 8·2%). λ_{max} ($CHCl_3$) 340 nm (ϵ 20000). ν_{max} 1600, 1520, 1355, 1035 cm^{-1}. *m/z* 432 (M, 54%), 417 (38), 401 (29), 397 (30), 355 (20), 347 (47), 335 (48), 329 (31), 321 (44), 133 (26), 69 (77), 57 (32), 55 (45), 43 (100), 41 (53). δ_H 0·93, s, $(H19)_3$; 0·95, s, $(H18)_3$; 1·18, s, $(H20)_3$; 1·20, ddd, $J_{3\alpha,3\beta}$ 13·3, $J_{3\alpha,2\beta}$ 13·3, $J_{3\alpha,2\alpha}$ 4·7 Hz, H3α; 1·23, dd, $J_{5\alpha,6\beta}$ 12·7, $J_{5\alpha,6\alpha}$ 2·3 Hz, H5; 1·33, ddd, $J_{1\alpha,1\beta}$ 12·9, $J_{1\alpha,2\beta}$ 12·9, $J_{1\alpha,2\alpha}$ 4·0 Hz, H1α; 1·33, 1·34, 2d, $J_{16,15} = J_{17,15}$ 6·6 Hz, $(H16)_3$, $(H17)_3$; 1·48, dm, $J_{3\beta,3\alpha}$ 13·3 Hz, H3β; 1·56–1·70, m, H2α, H6β; 1·74, ddddd, $J_{2\beta,2\alpha}$ 13·6, $J_{2\beta,3\alpha}$ 13·3, $J_{2\beta,1\alpha}$ 12·9, $J_{2\beta,3\beta}$ 3·2, $J_{2\beta,1\beta}$ 3·2 Hz, H2β; 1·94, dd, $J_{6\alpha,6\beta}$ 13·3, $J_{6\alpha,7\alpha}$ 8·0 Hz, H6α; 2·33, dm, $J_{1\beta,1\alpha}$ 12·9 Hz, H1β; 2·35, s, COMe; 2·81, ddd, $J_{7\alpha,7\beta}$ 18·1, $J_{7\alpha,6\beta}$ 10·1, $J_{7\alpha,6\alpha}$ 8·0 Hz, H7α; 2·99, dd, $J_{7\beta,7\alpha}$ 18·1, $J_{7\beta,6\beta}$ 6·2 Hz, H7β; 3·34, m, H15; 3·69, s, OMe; 6·87, s, COC**H**COMe; 7·75, s, H11. δ_C 18·91, 19·13, C2, C6; 21·40, C16; 21·40, C17; 21·52, C19; 24·46, 24·78, C20, CO**Me**; 27·32, C15; 29·32, C7; 33·08, C18; 33·29, C4; 38·12, C10; 39·27, C1; 41·33, C3; 49·15, C5; 63·42, OMe; 101·25, CO**C**HCOMe; 123·02, s, aryl C; 126·01, C11; 139·88, s, aryl C; 143·44, s, aryl C; 147·16, s, aryl C; 183·51, s, aryl C; 191·07, s, aryl C. *m/z* 432 (M, 54%), 417 (38), 401 (29), 397 (30), 355 (20), 347 (47), 335 (48), 329 (31), 321 (44), 133 (26), 69 (77), 57 (32), 55 (45), 43 (100), 41 (53).

(B) Boron trifluoride etherate (*c.* 45% BF_3, 0·5 ml, 3·5 mmol) was added to a cooled (0°) solution of the ether (4) (0·20 g, 0·67 mmol) in acetic anhydride (10 ml) and the mixture was stirred at room temperature under nitrogen. After 4 h and after 20 h additional reagent (0·5 ml) was added. After 27 h the mixture was worked up to give an oil which was chromatographed (p.l.c.) on silica and eluted with hexane/ether (6 : 1). A band, R_F 0·8, gave 12-acetyltotara-8,11,13-trien-13-ol (8) (50%) (identical ^1H n.m.r. spectrum). A band, R_F 0·3, gave the chelate (26) (24%) (identical ^1H n.m.r. spectrum).

4-(13-Methoxytotara-8,11,13-trien-12-yl)butane-2,4-dione (10)

Hydrogen peroxide (30%, 30 μl, 0·28 mmol) was added dropwise to a solution of the chelate (26) (60 mg, 0·14 mmol) in methanol (20 ml) and the solution was stirred at room temperature under argon for 48 h. The mixture was diluted with ether (40 ml) and washed with water and brine and dried. Removal of the solvent under reduced pressure gave an oil which was chromatographed (p.l.c.) on silica. Elution with hexane/ether (9 : 1) gave a band, R_F 0·6, which afforded *4-(13-methoxytotara-8,11,13-trien-12-yl)butane-2,4-dione* (16 mg, 30%) as a clear oil, b.p. (Kugelrohr) 120°/0·05 mm (Found: C, 77·6; H, 9·6. $C_{25}H_{36}O_3$ requires C, 78·1; H, 9·4%). ν_{max} 3750–3100 (OH), 1605 (CO), 1520 cm^{-1}. δ_H 0·92, s, $(H19)_3$; 0·95, s, $(H18)_3$; 1·19, s, $(H20)_3$; 1·22, m, H3α; 1·25, dd, $J_{5\alpha,6\beta}$ 12·6, $J_{5\alpha,6\alpha}$ 2·1 Hz, H5; 1·33, 1·35, 2d, $J_{16,15} = J_{17,15}$ 6·5 Hz, $(H16)_3$, $(H17)_3$; 1·36, ddd, $J_{1\alpha,1\beta}$ 13·1, $J_{1\alpha,2\beta}$ 13·1, $J_{1\alpha,2\alpha}$ 3·7 Hz, H1α; 1·48, br d, $J_{3\beta,3\alpha}$ 13·0 Hz, H3β; 1·56–1·70, m, H2α, H6β; 1·74, ddddd, $J_{2\beta,2\alpha}$ 13·6, $J_{2\beta,1\alpha}$ 13·1, $J_{2\beta,3\alpha}$ 13·0, $J_{2\beta,1\beta}$ 3·2, $J_{2\beta,3\beta}$ 3·2 Hz, H2β; 1·92, dd, $J_{6\alpha,6\beta}$ 13·2, $J_{6\alpha,7\beta}$ 7·9 Hz, H6α; 2·16, s, Me; 2·31, br d, $J_{1\beta,1\alpha}$ 13·1 Hz, H1β; 2·78, m, H7α; 2·95, dd, $J_{7\beta,7\alpha}$ 17·9, $J_{7\beta,6\beta}$ 5·9 Hz, H7β; 3·32, m, H15; 3·69, s, OMe; 6·25, s, 1H, =C**H**OH; 7·46, s, H11. δ_C 19·14, 19·30, C2, C6; 21·49, C16; 21·49, C17; 21·56, C19; 24·92, C20; 25·20, Me; 27·50, C15; 29·03, C7; 33·16, C18; 33·30, C4; 38·01, C10; 39·87, C1; 41·45, C3; 49·33, C5; 62·39, OMe; 100·85, CH; 124·47, C11; 127·07, aryl C; 138·89, aryl C; 146·13, aryl C; 163·0, aryl C; 191·57, CO. *m/z* 384 (M, 12%), 369 (M−Me, 10), 353 (M−OMe, 100), 273 (12), 69 (15).

Elbs Persulfate Oxidation of Totarol (1)

A saturated solution of ammonium persulfate (80 mg) was added dropwise over 10 min to a solution of totarol (0·10 g, 0·35 mmol) in aqueous sodium hydroxide (5% w/v, 3 ml) and

pyridine (7 ml), and the mixture was stirred at room temperature under argon for 19 h. The mixture was diluted with ether (40 ml), washed with dilute hydrochloric acid (30 ml), water (30 ml), and brine (30 ml), and solvent was removed from the dried solution under reduced pressure to give a foam. The product was purified by flash chromatography on silica gel with hexane as eluent to give podototarin (24) (68 mg, 68%) which crystallized from hexane as microrods, m.p. 220·5–221° (lit.[17] 225–226°) (correct i.r. and ^{1}H n.m.r. spectra[17]). δ_C 19·33, 19·42, C2, C6; 20·15, C19; 21·57, C16, C17; 25·21, C20; 25·45, C20′; 27·71, C15; 28·72, C7; 28·90, C7′; 33·24, C18; 33·28, C4; 37·80, C10; 39·54, C1; 39·64, C1′; 41·54, C3; 49·55, C5; 49·62, C5′; 120·76, C8; 124·40, C11; 131·98, C12; 134·68, C14; 143·29, C9; 149·81, C13.

Reaction of Totarol (1) with Copper(II) Nitrate

A solution of totarol (0·10 g) in acetonitrile (10 ml) was treated with cupric nitrate trihydrate (85 mg) in acetonitrile (10 ml) and the mixture was stirred at room temperature for 15 min. Water was added and the mixture was extracted with chloroform. Workup of the organic layer gave 12-nitrototara-8,11,13-trien-13-ol (11) (58 mg, 50%), m.p. and mixed m.p. 71–72° (correct ^{1}H n.m.r. spectrum[1]).

Treatment of Totarol (1) with Cerium(IV) Ammonium Nitrate

A solution of totarol (0·10 g, 0·35 mmol) and sodium dodecyl sulfate (5 mg) in acetic acid (3 ml) was added to a solution of ceric ammonium nitrate (0·19 g, 0·35 mmol) in water (1 ml). Hydrogen peroxide (30%, 40 μl, 0·35 mmol) was added followed by acetic acid (3 ml), and the mixture was stirred at room temperature under nitrogen for 22 h. The mixture was worked up to give a semisolid which was chromatographed (p.l.c.) on silica and eluted with hexane/ether (5 : 1). A predominant yellow band afforded 12-nitrototara-8,11,13-trien-13-ol (50 mg, 43%), m.p. and mixed m.p. 71–72° (correct ^{1}H n.m.r. spectrum[1]). *m/z* 331 (M, 42%), 317 (21), 316 (100), 260 (10), 248 (11), 247 (16), 246 (75), 235 (12), 234 (85), 220 (68), 84 (70), 69 (85), 41 (45).

Demethylation of 13-Methoxytotara-8,11,13-trien-12-ol (12)

A solution of the phenol (12) (0·10 g) and sodium iodide (0·19 g) in dry acetonitrile (7·5 ml) was heated under reflux under argon for 10 min. Chlorotrimethylsilane (0·09 ml) was added and the refluxing was continued for 27·5 h. The reaction was quenched with water and the product was extracted into ether. The organic layer was washed with sodium thiosulfate and worked up to give an oil which was chromatographed (p.l.c.) on silica under argon. Elution with dichloromethane saturated with argon gave four bands. A band, R_F 0·41, was extracted into dichloromethane and the solvent was removed under vacuum to give *totara-8,11,13-triene-12,13-diol* (2) (81 mg, 85%) as a yellow oil, b.p. 110°/0·08 mm (Found: C, 79·2; H, 10·1. $C_{20}H_{30}O_2$ requires C, 79·4; H, 10·1%). ν_{max} 3600–3150 (OH), 1605 cm^{-1} (C=C). δ_H 0·90, 0·94, 2s, (H18)$_3$, (H19)$_3$, (H20)$_3$; 1·35, d, *J* 7·5 Hz, (H16)$_3$, (H17)$_3$; 3·15, sept., *J* 7·5 Hz, H15; 4·84, 5·15, 2 br s, OH (D_2O exchanged); 6·60, br s, H11. The peak at 6·60 sharpened and intensified on D_2O exchange. *m/z* 302 (M, 85%), 287 (100), 245 (7), 217 (41), 205 (19), 191 (66), 175 (10), 69 (36), 55 (26), 40 (49).

Attempted ozonolysis of (2) in chloroform/methanol (1 : 1) with an excess or 1 equiv. of ozone gave a mixture of at least 10 products.

Oxidation of 13-Methoxytotara-8,11,13-trien-12-ol (12)

2,3-Dichloro-5,6-dicyanobenzoquinone (45 mg) was added to a solution of the phenol (12) (56 mg) in anhydrous methanol (7 ml) and the mixture was stirred under argon at 20° for 2 h. The mixture was diluted with dichloromethane (10 ml) and washed successively with 5% aqueous sodium hydroxide, saturated sodium hydrogencarbonate, water, and brine. Solvent was removed from the dried organic layer under vacuum to give an oil which was

chromatographed (p.l.c.) on silica gel. Elution with dichloromethane gave one main band, R_F 0·33–0·10, which afforded *13,13-dimethoxytotara-8(14),9(11)-dien-12-one* (27) (42 mg, 68%) as a yellow oil which after Kugelrohr distillation (70°/0·02 mm) gave a crystalline solid (Found: C, 76·2; H, 10·1. $C_{22}H_{34}O_3$ requires C, 76·0; H, 10·2%). ν_{max} 1660 (C=O), 1060 cm^{-1} (C–O). δ_H 0·89, s, $(H19)_3$; 0·93, s, $(H18)_3$; 1·17, s, $(H20)_3$; 1·10–1·18, m, 1H; 1·24, d, $J_{16,15} = J_{17,15}$ 7·2 Hz, $(H16)_3$, $(H17)_3$; 1·30–1·47, m, 2H; 1·53–1·70, m, 4H; 1·75–1·93, m, 2H; 2·73, t, J 7·4 Hz, 2H; 3·07, sept., $J_{15,16} = J_{15,17}$ 7·2 Hz, H15; 3·16, 3·21, 2s, 2OMe; 5·87, s, H11. δ_C 18·86, 19·10, C2, C6; 21·35, 21·40, C16, C17; 21·76, C19; 22·49, C20; 25·12, C7; 27·69, C15; 32·56, C18; 34·13, C4; 38·58, C1; 39·51, C10; 41·34, C3; 46·26, C5; 50·67, OMe; 51·01, OMe; 94·34, C13; 117·26, C11; 132·48, C8; 148·77, C9; 169·08, C14; 197·43, C12. *m/z* 346 (M, 19%), 331 (56), 316 (12), 303 (100), 272 (27), 243 (24), 105 (18), 91 (21), 69 (32), 55 (34), 41 (52).

Treatment of 12-Bromo-13-methoxytotara-8,11,13-triene (14) with Copper(I) Iodide

Copper(I) iodide (48 mg, 0·25 mmol) and the bromo ether (14) (0·19 g, 0·5 mmol) were added to a mixture of sodium methoxide [from sodium (35 mg) and dry methanol (0·6 ml)], and 2,4,6-collidine (0·5 ml). Further collidine (2·5 ml) was added and the mixture was heated under reflux under nitrogen for 23 h. The cooled mixture was diluted with methanol (5 ml) and poured into 5 mol l^{-1} hydrochloric acid. Extraction with ether and workup of the extracts gave 13-methoxytotara-8,11,13-triene (4) (0·16 g, 100%) as a crystalline solid (identical ^1H n.m.r. spectrum).

Repetition of the above experiment, replacing methanol with propan-1-ol gave a mixture (1 : 1) of starting material and (4) (^1H n.m.r. analysis).

Tricarbonyl[(8,9,11,12,13,14-η)-13-methoxytotara-8,11,13-triene]chromium(0) (28) and (29)

A solution of 13-methoxytotara-8,11,13-triene (4) (1·0 g, 3·33 mmol) in dibutyl ether (8 ml) and dry tetrahydrofuran (2·5 ml), was treated with hexacarbonylchromium(0) (0·81 g, 3·7 mmol) and the mixture was degassed by bubbling with dry argon for 10 min. An argon bubbler was attached to the top of the condenser, the flask was covered with foil, and the mixture was heated under reflux for 23 h. The cooled solution was filtered through a Celite pad which was then washed with ether (250 ml). Removal of solvent from the combined filtrates under vacuum gave a yellow solid which was flash chromatographed on silica in a light-protected column as rapidly as possible. Elution with hexane gave starting material (0·49 g, 49%). Elution with hexane/ether (9 : 1) gave a mixture of the α and β diastereomers (28) and (29) (56 : 44) of *tricarbonyl[(8,9,11,12,13,14-η)-13-methoxytotara-8,11,13-triene]chromium(0)* (0·74 g, 51%), which formed yellow prisms from hexane/ethyl acetate, m.p. 184–186° (Found: C, 66·0; H 7·5. $C_{24}H_{32}CrO_4$ requires C, 66·0; H, 7·4%). ν_{max} (film) 1922 (C≡O), 1860 (C≡O), 1840 (C≡O), 1235 cm^{-1} (C–O–C). δ_H (C_6D_6) α-diastereomer: 0·74, s, $(H20)_3$; 0·92, s, $(H19)_3$, $(H18)_3$; 1·14, dd, J 6·3, 6·2 Hz, $(H16)_3$, $(H17)_3$, 3·06, s, $(H21)_3$; 4·02, d, J 7·2 Hz, H11; 5·19, d, J 7·3 Hz, H12; β-diastereomer: 0·72, s, $(H19)_3$; 0·78, s, $(H18)_3$; 1·22, s, $(H20)_3$; 1·57, dd, J 6·3, 5·2 Hz, $(H16)_3$, $(H17)_3$; 3·05, s, $(H21)_3$; 4·16, d, J 7·3 Hz, H11; 5·26, d, J 7·3 Hz, H12. δ_C (CCl_4) α-diastereomer: 18·27, C2; 18·69, C6; 20·06, C15; 20·91, C16, C17; 25·50, C20; 26·09, C7; 32·76, C18; 33·01, C4; 36·41, C10; 38·18, C1; 40·76, C3; 47·21, C5; 54·84, C21; 71·21, C12; 91·03, C11; 112·71, C14; 117·01, C9; 234·90, CO; β-diastereomer: 18·00, C2; 19·76, C6; 21·28, C16, C17; 27·03, C15; 27·41, C20; 30·69, C7; 32·76, C4; 32·94, C18; 36·53, C10; 40·55, C1; 40·64, C3; 50·75, C5; 54·72, C21; 70·60, C12; 93·02, C11; 234·54, CO. δ_C (C_6D_6) α-diastereomer: 18·79, C2; 19·27, C6; 20·39, C15; 21·27, C16, C17; 25·68, C20; 26·49, C7; 33·09, C4; 33·13, C18; 36·83, C10; 38·74, C1; 41·18, C3; 47·75, C5; 54·73, C21; 71·39, C12; 91·16, C11; 112·63, C14; 117·00, C9; 143·26, C13; 235·55, CO; β-diastereomer: 18·52, C2; 20·27, C6; 21·61, C16, C17; 27·53, C15; 25·68, C20; 26·49, C7; 33·29, C18; C4; 36·90, C10; 40·89, C1; 41·02, C3; 51·24, C5; 54·65, C21; 70·82, C12; 93·18, C11; 112·43, C14; 118·86, C9; 143·07 C13; 235·16, CO. *m/z* 436 (M, 7%), 380 (M−2CO, 7), 352 (M−3CO, 100), 300 (352−Cr, 12), 285 (300−Me, 28) 215 (285−C_5H_{10}, 9), 189 (285−C_7H_{12}, 14), 69 (C_5H_9, 7), 52 (Cr, 20).

13-Methoxytotara-8,11,13-trien-12-ol (12)

(A) Tricarbonyl [(8,9,11,12,13,14-η)13-methoxytotara-8,11,13-triene]chromium(0) (28) and (29) (0·20 g, 0·67 mmol) in tetrahydrofuran (10 ml) and *N,N,N′,N′*-tetramethylethylenediamine (1·5 ml) were added through a syringe under vacuum to a flame-dried flask which contained a stirrer bar, was equipped with a serum cap, and had been flushed (×3) with argon from a reservoir on a side arm. The mixture was cooled to −78°, butyllithium in hexanes (1·65 ml, 2·0 mol l^{-1}, 3·3 mmol) was added dropwise and the solution was stirred for 1 h. The temperature was then raised to −40° and Mo**OPH** (2·9 g, 6·67 mmol) was added over 5 min, and the mixture was stirred at −40° for 4 h, and warmed to room temperature. Dilute aqueous sodium hydrogensulfite was added and the solution was diluted with ether (50 ml). The organic layer was washed with water, dried, and then left in sunlight with air bubbling through it for 4 h. The product was flash chromatographed on silica with hexane/ether (5 : 1) as eluent to give a mixture which was chromatographed (p.l.c.) with hexane/ether (9 : 1) as eluent to give in order of increasing polarity (i) 13-methoxytotara-8,11,13-triene (4) (16 mg, 12%), m.p. and mixed m.p. 92–93° (correct ^{1}H n.m.r. spectrum); and (ii) 13-methoxytotara-8,11,13-triene-12-ol (12) (24 mg, 18%) as white solid, m.p. and mixed m.p. 166–167·5° (correct i.r. and mass spectra). δ_H 0·91, s, (H19)$_3$; 0·94, s, (H18)$_3$; 1·12, s, (H20)$_3$; 1·28, d, *J* 2·2 Hz, H3α; 1·33, dd, *J* 7·1, 3·7 Hz, (H16)$_3$, (H17)$_3$; 1·38, d, *J* 3·5 Hz, H1α; 1·46, dq, *J* 13·2, 1·1 Hz, H3β; 1·58, dt, *J* 13·9, 3·7 Hz, H2α; 1·63, q, *J* 4·8 Hz, H6β; 1·72, qt, *J* 13·6, 3·3 Hz, H2β; 1·89, dd, *J* 14·1, 7·7 Hz, H6α; 2·17, dt, *J* 3·5 Hz, H1β; 2·70, m, H7α; 2·89, dd, *J* 16·8, 5·4 Hz, H7β; 3·34, br s, 3·25–3·40, H15; 3·77, s, 3H, ArOMe; 5·22, br s, 12-OH; 6·77, s, H11. δ_C 19·40, C2; 19·43, C6; 21·62, C16, C17, C19; 24·82, C20; 27·49, C15; 28·02, C7; 33·18, C18; 33·33, C10; 38·10, C4; 39·45, C1; 41·50, C3; 49·56, C5; 61·33, C21; 109·98, C11; 125·72, C8; 138·24, C14; 144·16, C9; 146·77, C12; 147·10, C13.

(B) Repetition of the experiment with lithium diisopropylamide (72 μl, 0·51 mmol) gave (i) 13-methoxytotara-8,11,13-triene (4) (40 mg, 43%); (ii) tricarbonyl[(8,9,11,12,13,14-η)13-methoxytotara-8,11,13-triene]chromium(0) (28,29) (27 mg, 14%); and (iii) a mixture of the diterpenoid complex and an unidentified diterpenoid (25 mg).

(C) Repetition of the experiment with the complex (28) and (29) (0·10 g, 0·23 mmol) in tetrahydrofuran (5 ml) and t-butyllithium (1·0 mol l^{-1} in pentane, 1·2 ml, 1·2 mmol) followed by Mo**OPH** (1·0 g, 2·3 mmol) gave (4) (39 mg, 57%), and (12) (18 mg, 25%).

(D) Repetition of the experiment (C) with the addition of copper(I) bromide/dimethyl sulfide complex (0·25 g, 1·2 mmol) after the t-butyllithium gave (4) (25 mg, 36%) and (12) (45 mg, 66%).

Treatment of the Complex (28) and (29) with Lithioacetonitrile and Iodine

Diisopropylamine (130 μl, 0·92 mmol) and tetrahydrofuran (5 ml) were added through an argon-purged syringe to a flask dried as above, and the solution was cooled to −78°. Butyllithium in hexanes (0·46 ml, 2·0 mol l^{-1}, 0·92 mmol) was added dropwise and the solution was stirred for 10 min. Acetonitrile (56 μl, 1·07 mmol) was added, the solution was stirred for 30 min, and then hexamethylphosphoric triamide (2·5 ml) and a solution of tricarbonyl[(8,9,11,12,13,14-η)-13-methoxytotara-8,11,13-triene]chromium(0) (28) and (29) (0·20 g, 0·46 mmol) in tetrahydrofuran (5 ml) was added dropwise and the solution was stirred at −78° for 6·5 h. Iodine (1·03 g, 4·05 mmol) in tetrahydrofuran (7 ml, precooled to −78°) was added and the solution was warmed to room temperature overnight. Workup gave an oil which was flash chromatographed on silica. Elution with hexane gave 13-methoxytotara-8,11,13-triene (5) (20 mg, 15%), and elution with hexane/diethyl ether gave, in order of elution (i) a clear oil (28 mg); (ii) 13-methoxytotara-8,11,13-trien-7α-ol (30) as a colourless solid (20 mg, 15%), m.p. 118–120°. An elemental analysis was not obtained. ν_{max} 3300 (br, OH), 1479 (aryl C=C), 1259, (C–O), 1049 cm^{-1} (C–O). δ_H 0·94, s, (H18)$_3$; 0·95, s, (H19)$_3$; 1·16, td, *J* 13·4, 4 Hz, H3α; 1·23, dd, *J* 13·7, 6·6 Hz, (H16)$_3$, (H17)$_3$; 1·31, td, *J* 12·9, 13·5 Hz, H3β; 2·23, d, *J* 12·4 Hz, H1β; 2·39, ddd, *J* 13·3, 9, 2·4 Hz, H6α; 3·50, quintet, *J* 7 Hz, H15; 3·79, s, (H21)$_3$; 5·14, t, *J* 8·5 Hz, H7β; 6·80, d, *J* 8·8 Hz, H12; 7·09, d, *J* 8·8 Hz, H11. *m/z* 316 (M, 24%), 298 (M−H_2O, 35), 283 (298−Me, 100), 241 (283−C_3H_6), 69 (C_5H_9, 27); and (iii) an unidentified white solid (28 mg).

12-Iodo-13-methoxytotara-8,11,13-triene (31)

Mercury(II) oxide/tetrafluoroboric acid on silica gel (1·65 g) and iodine (85 mg, 0·33 mmol) were added to 13-methoxytotara-8,11,13-triene (4) (0·20 g, 0·67 mmol) in 1,2-dichloroethane (10 ml) with rapid stirring, and the mixture was stirred at 85° for 10 h. The cooled mixture was diluted with ether, the mercury salts were removed, and the filtrate was washed with 5% aqueous sodium hydrogensulfite, water, and brine (25 ml). Solvent was removed under vacuum from the dried solution and the product was chromatographed (p.l.c.) on silica. Elution with hexane gave, in order of elution, starting material (63 mg, 32%) and *12-iodo-13-methoxytotara-8,11,13-triene* (90 mg, 32%) as clear needles (from hexane), m.p. 122–124° (Found: C, 59·4; H, 7·1%; $M^{+\bullet}$, 426.1447. $C_{21}H_{31}IO$ requires C, 59·2; H, 7·3%; $M^{+\bullet}$, 426·1420). ν_{max} 1456 (aryl C=C), 1249 (C–O), 1007 cm^{-1} (C–O). δ_H 0·91, s, $(H19)_3$; 0·94, s, $(H18)_3$; 1·17, s, $(H20)_3$; 1·19, td, *J* 9·2, 3·7 Hz, H3α; 1·23, dd, *J* 12·8, 2·4 Hz, H5α; 1·31, dd, *J* 7·1, 4·6 Hz, $(H16)_3$, $(H17)_3$; 1·35, td, *J* 13, 3·9 Hz, H1α; 1·47, d, *J* 13·3 Hz, H3β; 1·59, dt, *J* 10·2 Hz, H2α; 1·65, q, *J* 6·7 Hz, H6β; 1·72, qt, *J* 13·7, 3.3 Hz, H2β; 1·89, dd, *J* 13·3, 7·9 Hz, H6α; 2·17, d, *J* 12·5 Hz, H1β; 2·72, m, H7α; 2·90, dd, *J* 17·5, 6·1 Hz, H7β; 3·33, br s, 3·22–3·43, H15; 3·76, s, $(H21)_3$; 7·48, s, H11. δ_C 19·14, C6; 19·30, C2; 21·55, 21·63, C16, C17; 24·86, C20; 27·86, C15; 28·42, C7; 33·13, C18, 33·29, C4; 37·97, C10; 39·40, C1; 41·39, C3; 49·29, C4; 37·97, C10; 39·40, C1; 41·39, C3; 49·29, C5; 61·82, C21; 39·53, C12; 134·15, C11; 135·44, C8; 139·0, C14; 148·73, C9; 156, C13. *m/z* 426 (M, 100%), 411 (M–Me, 70), 341 (411–C_5H_{10}, 44), 329 (M–C_7H_{13}, 50), 315 (411–C_7H_{12}, 66), 184 (M–I, 13), 69 (C_5H_9, 46).

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