Total Synthesis of (±)-Pisiferic Acid †

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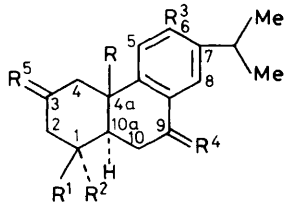
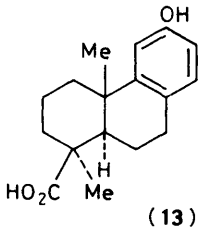
A total synthesis of (±)-pisiferic acid (**1**) has been achieved by utilising the keto ether (**22**) which, in turn, was prepared from the alcohol (**14**). Subjection of the keto ether (**22**) to three sequential reactions (formylation, Michael addition with methyl vinyl ketone, and intramolecular aldol condensation) provided the tricyclic ether (**27**) whose conversion into the methoxyabietatriene (**32**) was accomplished in four steps (ethoxycarbonylation, Grignard reaction with methyl-lithium, acid-catalysed dehydration, and methoxylation). Reaction of the methoxyabietatriene (**32**) with zinc, zinc iodide, and acetic acid produced (±)-pisiferol (**2**) which was finally converted into (±)-pisiferic acid (**1**). The ketone (**34**) was converted into the abietatriene (**41**) following exactly the same procedure adopted for the transformation of the keto ether (**22**) into the abietatriene (**32**). Hydroboration–oxidation of (**41**) followed by oxidation with Jones reagent and reduction with lithium aluminium hydride followed by transannular oxidation gave the abietatriene (**36**).

Pisiferic acid (**1**), an abietane type diterpene acid, was first isolated [1] from the methanolic extract of leaves and twigs of *Chamaecpyparis pisifera* Endle whose timber has been found to





(**13**)

(**1**) R = COOH, $R^1 = R^2$ = Me, R^3 = OH, $R^4 = R^5$ = H, H
(**2**) R = CH_2OH, $R^1 = R^2$ = Me, R^3 = OH, $R^4 = R^5$ = H, H
(**3**) R = CO_2Me, $R^1 = R^2$ = Me, R^3 = OH, $R^4 = R^5$ = H, H
(**4**) R = CO_2H, $R^1 = R^2$ = Me, R^3 = OMe, $R^4 = R^5$ = H, H
(**5**) R = CHO, $R^1 = R^2$ = Me, R^3 = OH, $R^4 = R^5$ = H, H
(**6**) R = $R^1 = R^2$ = Me, R^3 = OH, $R^4 = R^5$ = H, H
(**7**) R = R^1 = Me, $R^2 = CO_2H$, $R^3 = R^4 = R^5$ = H, H
(**8**) R = CH_2OH, $R^1 = R^2$ = Me, R^3 = OMe, $R^4 = R^5$ = H, H
(**9**) R = CO_2Me, $R^1 = R^2$ = Me, R^3 = OMe, R^4 = O, R^5 = H, H
(**10**) R = CO_2Me, $R^1 = R^2$ = Me, R^3 = OMe, $R^4 = R^5$ = H, H
(**11**) R = $R^1 = R^2$ = Me, R^3 = OMe, R^4 = H, H, R^5 = ~OH, H
(**12**) R = $R^1 = R^2$ = Me, R^3 = OMe, R^4 = H, H, R^5 = 

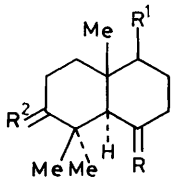
be one of the best materials for rice chests. The isolation and structural studies of related diterpenoids, possessing angular oxygenated methyl groups, pisiferol (**2**), methyl pisiferate (**3**), *O*-methyl pisiferic acid (**4**), and pisiferal (**5**) were also reported by Yatagai and Takahashi.[2,3] Pisiferic acid (**1**) and ferruginol (**6**) showed antimicrobial activity especially against all gram-positive bacteria tested while dehydroabietic acid (**7**) and podocarpic acid (**13**) showed little or no such activity.

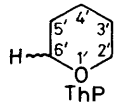
These observations led to the following conclusions.[1] (*i*) The isopropyl group on the aromatic ring was responsible for the biological activity of pisiferic acid (**1**) and the ferruginol (**6**). (*ii*) An enhancement in biological activity was observed when the isopropyl and hydroxy groups were *ortho* to each other. (*iii*) The presence of a carboxy group in ring A decreases the activity of diterpenoids.

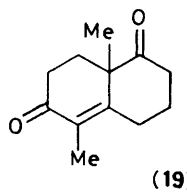
Recently Matsumoto and Usui reported the total synthesis [4] of (±)-pisiferic acid. The synthesis of natural pisiferol (**2**) has also been reported independently by Matsumoto [5] and Uda.[6] In connection with our research towards the synthesis of terpenoid compounds and in view of the antimicrobial activity of pisiferic acid (**1**), an alternative convenient route for this important molecule was explored. The present paper gives details of the investigation which led to the total synthesis [7] of (±)-pisiferic acid (**1**).

Our synthetic approach to pisiferic acid centred around the following. (*a*) Construction of the ether (**22**) and its transformation to the keto ether (**27**). (*b*) Introduction of a 2-hydroxypropan-2-yl side-chain at C-2 of the keto ether (**27**) and its conversion into the hydroxyabietatriene (**31**) by dehydration and acid-catalysed aromatisation. (*c*) Cleavage of the ether bridge to introduce the hydroxymethylene group in an angular position whose conversion into a carboxylic acid would lead to the desired molecule pisiferic acid (**1**).

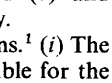
Our starting point was the already reported [8] alcohol (**14**) which was converted into the ketone (**15**) by oxidation with Sarett's reagent.[9] Reduction of the ketone (**15**) with lithium







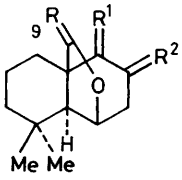
(**19**)

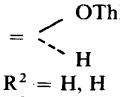
(**14**) R =  , R^1 = OThP, R^2 = H, H
(**15**) R = O, R^1 = OThP, R^2 = H, H
(**16**) R =  , R^1 = OThP, R^2 = H,H
(**17**) R = H, H, R^1 = H, R^2 = O
(**18**) R = H, H, R^1 = OThP, R^2 = O

† Part of this work was presented (A. K. B.) at the Fifteenth International Congress on Natural Products, Den Haag, Holland, August 17—22, 1986.

aluminium hydride yielded the alcohol (**16**) in 56% yield. Measurement of the 1-H peak width ($W_{\frac{1}{2}}$) proved difficult since it was obscured by 2′-H and 4-H; the configuration of the 1-hydroxy group could not, therefore, be established at this stage. However, the comparison of the ^{1}H n.m.r. data of the alcohols (**14**) and (**16**) showed that the 1-hydroxy group of the alcohol (**16**) has the axial configuration; this stereochemical assignment was subsequently confirmed.

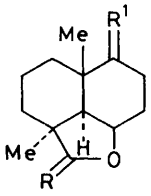
Irradiation of a cyclohexane solution of the alcohol (**16**) with lead tetra-acetate and iodine [10] afforded, as expected, two cyclic ethers in 45 and 10% yields to which the structures (**20**) and

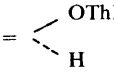


(**20**) R = H, H, R^1 =  , R^2 = H, H
(**21**) R = R^1 = O, R^2 = H, H
(**22**) R^1 = O, R = R^2 = H, H
(**23**) R = H, H, R^1 = O, R^2 = CHOH

(**24**) were assigned respectively, by analogy with earlier results.[11] It is worthwile mentioning that the yield of the cyclic ether (**24**) was not reproducible and varied from run to run. The spectroscopic evidence (see Experimental section) did not unequivocally differentiate the cyclic ether (**20**) from the cyclic ether (**24**) and thus it was necessary to obtain chemical evidence for the rigorous assignment of the two structures.

Treatment of the cyclic ether (**20**) with chromium trioxide in acetic acid at room temperature yielded the lactone (**21**) in satisfactory yield whose spectral properties agreed with the assigned structure. Similarly, the cyclic ether (**24**) was converted into the lactone (**25**) whose alternative synthesis has also been

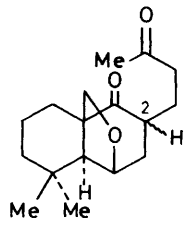


(**24**) R^1 =  , R^2 = H, H
(**25**) R^1 = R = O

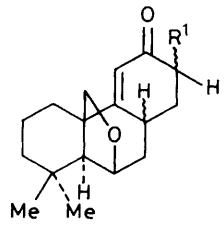
reported.[12] The lactonic structure and compound (**25**) was confirmed by spectroscopic analysis and mixed melting point measurement with an authentic sample.[12] These observations not only confirmed the structures of the cyclic ether (**24**) and the lactone (**25**) but also confirmed our assumption regarding the structure of the cyclic ether (**20**) and the lactone (**21**).

Having successfully established the structure of the cyclic ether (**20**) we next focussed our attention on its conversion into the tricyclic keto ether (**27**) as follows. The cyclic ether (**20**), on oxidation with Jones reagent [13] at 0 °C, afforded the keto ether (**22**) which on treatment with ethyl formate produced the formyl derivative (**23**) in satisfactory yield and this was subjected to Robinson annelation with 4-diethylaminobutan-2-one methiodide following the procedure of Howell and Taylor.[14] The oily adduct (**26**) proved to be a mixture of C-2 epimers as shown by the appearance of two singlets for acetyl groups, (δ_H 2.06 and 2.08). The adduct, when heated with sodium methoxide in methanol afforded the tricyclic keto ether (**27**) whose ^{1}H n.m.r. spectrum showed it to be a mixture of C-10a epimers. The completion of the synthesis of pisiferic acid (**1**) did not require the separation of α- and β-epimers and thus the keto ether (**27**) was used for the next step.

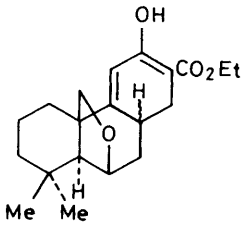
With the tricyclic nucleus of pisiferic acid successfully



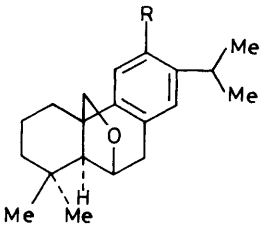
(**26**)



(**27**) R = H,H
(**28**) R = CO_2Et
(**29**) R = CMe_2OH



(**30**)



(**31**) R = OH
(**32**) R = OMe

constructed, an attempt was made to introduce an α-isopropyl functionality into the keto ether (**27**). A variety of methods were tried, the most effective and reproducible of which proved to be treatment of the keto ether (**27**) with diethyl carbonate in the presence of sodium hydride in 1,2-dimethoxyethane. The keto ether (**28**), obtained in moderate yield, had a complicated ^{1}H n.m.r. spectrum probably because of contamination with a small amount of the enol tautomer (**30**) whose formation was likely. Direct reaction of the keto ether (**28**) with methyl-lithium in ether produced an oily alcohol (**29**) which, on being refluxed with methanolic hydrochloric acid (10%), afforded a crystalline solid whose mass spectrum showed a base peak at m/z 300 and i.r. spectrum the presence of hydroxy absorption. One doublet at δ 1.26 (6 H, J 6 Hz) and two singlets at δ 6.62 (1 H) and δ 6.84 (1 H) were assigned to two methyl groups and two aromatic protons, respectively. These spectroscopic data can be explained if the structure (**31**) is assigned to the crystalline solid.

It now remained to convert the phenol (**31**) into pisiferic acid (**1**) and to realize this objective the former was methylated with dimethyl sulphate and sodium hydroxide to obtain (**32**). This protection was considered necessary because methods selected for the cleavage of the ether bridge of phenol (**31**) were expected to produce side products if the phenolic hydroxy group remained unprotected. A number of methods were sought but the most convenient and elegant consisted of heating compound (**32**) with zinc, zinc iodide, and acetic acid;[15] this produced pisiferol (**2**) whose melting point and spectroscopic data were found to be almost identical with the published data.[4] This reagent not only cleaved the ether bridge but also deprotected the product.*

In order to convert the pisiferol (**2**) into pisiferic acid (**1**), the former was subjected to oxidation with several oxidizing agents such as hydrated copper permanganate in dichloromethane,[16] solid sodium permanganate,[17] and potassium rutherate,[18] none of which were successful. It seemed that, owing to steric

* The identity of the pisiferol (**2**) could not be confirmed by direct comparison owing to the non-availability of an authentic specimen.

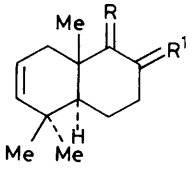
crowding, the angular hydroxymethylene group of pisiferol (**2**) did not yield to these reagents. Finally, the desired transformation was tried with Jones reagent at room temperature after protection of the phenolic hydroxy group as its methyl ether. Treatment of pisiferol (**2**) with dimethyl sulphate and sodium hydroxide yielded the methyl ether derivative (**8**) which on oxidation with Jones reagent at room temperature for 2 h afforded an acidic material which, without purification, was esterified with diazomethane. The product obtained was characterized as the keto ester (**9**) on the basis of its spectroscopic data and mixed melting point measurement with an authentic sample.[4] Extension of the oxidation reaction period (4—6 h) led to the formation of many side products which reduced the yield of the desired keto ester (**9**) considerably.

Finally the conversion of the keto ester (**9**) into pisiferic acid (**1**) was accomplished without any difficulty by reduction of the C-9 carbonyl of the keto ester (**9**) with sodium borohydride in methanol. This yielded, as expected, an alcoholic material whose *p*-tolylsulphonyl derivative, on heating with sodium iodide and zinc dust in dimethoxyethane,[19] produced the ester (**10**) whose identity was confirmed by comparing its spectral data and melting point with an authentic sample.[4] The transformation of the ester (**10**) to pisiferic acid (**1**) was achieved by two methods. The first procedure consisted of treatment of the ester (**10**) with anhydrous aluminium bromide and ethanethiol[20] which provided pisiferic acid (**1**) in excellent yield. The identity of the product was confirmed by comparison of its spectroscopic properties (i.r. and n.m.r.) with those already reported[4] and by mixed melting point and t.l.c. measurements with an authentic sample.[4]

The second method consisted of heating the ester (**10**) with quinoline and acetic acid.[21] The crude acidic product which exhibited weak signals for the methoxy group in the ^{1}H n.m.r. spectrum was subjected without purification to demethylation[22] with boron tribromide in dichloromethane to give the pisiferic acid (**1**) in moderate yield. The reason for not obtaining pisiferic acid (**1**) in satisfactory yield is probably due to the decarboxylation that occurred during heating with quinoline.

In 1982 Matsumoto and Usui[4] reported the conversion of the abietatriene (**36**) into pisiferic acid (**1**). In connection with our research on the synthesis of pisiferic acid (**1**), we explored an alternative and convenient synthetic route to compound (**36**) which could constitute a formal total synthesis of pisiferic acid (**1**). The important features of the present synthesis are the easy availability of the starting material and stereoselectivity in most of the steps involved.

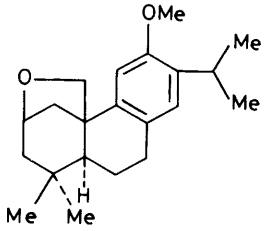
The keto alcohol (**17**)[23] prepared from the α,β-unsaturated ketone (**19**)[24] was the starting point for our synthetic approach. Treatment of the keto alcohol (**17**) with dihydropyran containing toluene-*p*-sulphonic acid yielded the oily pyranyl derivative (**18**). Reduction of the C-2 carbonyl group of (**18**) with sodium borohydride provided a mixture of alcohols whose *p*-tolylsulphonyl derivatives, on heating with lithium bromide, lithium carbonate, and dimethylformamide, afforded the oily olefin (**33**) the spectroscopic data of which confirmed the assigned structure. These conditions not only provoked the dehydrosulphonation but also the hydrolysis of the tetrahydropyranyl group, thus shortening the reaction sequence by one step. The oily ketone (**34**), obtained by oxidation of the olefin (**33**) with Jones reagent at room temperature, was condensed with ethyl formate to give the formyl derivative (**35**), a semi-solid dark material. This was subjected to Robinson annelation with 4-diethylaminobutan-2-one to introduce the oxobutyl side-chain and thereby obtain the keto ester (**37**). The product was contaminated with two other products but their R_F values on t.l.c. were very close and thus they could not be separated by any chromatographic technique. The adduct (**37**) on heating with sodium methoxide in methanol afforded the tricyclic enone (**38**) in 40% yield, a pivotal compound for its elaboration to abietatriene (**36**). The yield of enone was considerably improved when the adduct (**37**) was heated with sodium hydride in dimethoxyethane. The enone (**38**) proved to be a mixture of epimers at C-10a on the basis of the ^{1}H n.m.r. spectrum which exhibited more than three methyl groups. The region δ 5.55—5.72 p.p.m. indicated the presence of more than three protons. Since the synthesis of the abietatriene (**36**) was our goal, the separation of the epimers was considered unnecessary because both epimers would lead finally to the same product.



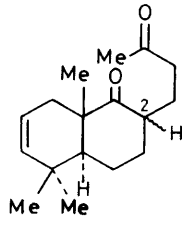
(**33**) R =  , R^1 = H,H

(**34**) R = O, R^1 = H,H

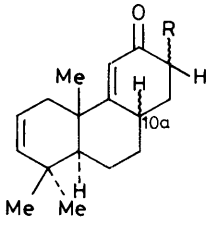
(**35**) R = O, R^1 = CHOH



(**36**)

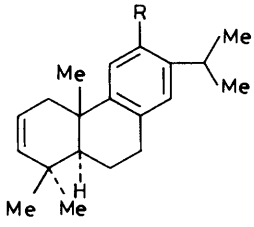


(**37**)



(**38**) R = H

(**39**) R = ~~CO_2Et



(**40**) R = OH

(**41**) R = OMe

The next phase of our studies consisted of the introduction of the isopropyl group at the C-2 position of the enone (**38**) and to accomplish this task it was treated with diethyl carbonate in the presence of sodium hydride to yield the β-keto ester (**39**). No attempt was made to determine the configuration of the ester group. Treatment of the keto ester (**39**) with methyl-lithium in ether afforded an oily alcoholic material which gave strong bands for hydroxy and α,β-unsaturated ketone groups in its i.r. spectrum. The alcoholic material on heating under reflux with methanolic hydrochloric acid (1%) led to the formation of a mixture of products which were eventually purified by column chromatography. The major product obtained was identified as the hydroxyabietatriene (**40**) on the basis of spectroscopic data (i.r. and ^{1}H n.m.r.) but it was contaminated with by-products as evidenced by t.l.c. which proved difficult to separate, its spectrum was, therefore, not well defined. In addition, the hydroxyabietatriene (**40**) proved to be an unstable compound whose colour rapidly changed within a few hours from yellow to dark red. It seemed to us that the aerial oxidation was responsible for this decomposition. In order to identify the hydroxyabietatriene (**40**) it was methylated with dimethyl sulphate–sodium hydroxide. The oily methoxyabietatriene, homogeneous by t.l.c., was assigned structure (**41**) on the basis of its spectral data (i.r., ^{1}H n.m.r., and m.s.). Identification of compound (**41**) also confirmed the identity of (**40**) which was formed during the acid-catalysed dehydration experiment. There is no doubt that the reaction of the keto ester (**39**) with methyl-lithium followed by acid hydrolysis proceeded with concomitant dehydration, migration of the double bond yielding the dienone which underwent aromatisation to give the phenol (**40**) in the same way as the formation of (**31**).

Attention was next focussed on the hydroxylation of the methoxyabeitatriene (**41**) to obtain compound (**42**) which would be required for the preparation of 2β,20β-epoxy-12-methoxyabietatriene (**36**); this transformation proved to be one of the most difficult parts of the present synthesis. A series of trials were made and the most satisfactory method involved the hydroboration–oxidation of the abietatriene (**12**) which yielded the alcohol (**11**). The ^{1}H n.m.r. spectrum of the hydroxy group of the alcohol (**11**) was not very clear and thus the configurational assignment of the C-2 proton of the alcohol (**11**) could not be confirmed on the basis of the half-width ($W_{\frac{1}{2}}$ value.[25] In order to determine the configuration of the hydroxy group of (**11**), the latter was oxidised with Jones reagent. The resulting ketone, without further purification, was reduced with $LiAlH_4$ in THF to give the alcohol (**12**) whose structural assignment was derived from its ^{1}H n.m.r. spectroscopic data. Irradiation of a mixture of the alcohol (**12**) and lead tetra-acetate in benzene with a 250 W tungsten lamp yielded the methoxyabietatriene (**36**) in 50% yield whose identity was established by direct comparison with an authentic specimen (i.r., t.l.c., mixed m.p.); its ^{1}H n.m.r. data were almost identical with those reported.[4] When the transannular oxidation was carried out in cyclohexane solution in the presence of lead tetra-acetate and iodine, the yield of abietatriene (**36**) was poor and a large amount of iodocyclohexane and other unidentified products were formed. As the abietatriene (**36**) has been previously converted into pisiferic acid (**1**), our alternative approach for the synthesis of (**36**) formally completes the synthesis of pisiferic acid (**1**).

We have already seen that abietatriene (**32**) when heated with zinc dust, zinc iodide, and acetic acid provided the pisiferol (**2**). Therefore we were interested in examining the behaviour of abietatriene (**36**) towards this reagent. In this case pisiferol (**2**) was also obtained and its conversion into pisiferic acid has already been mentioned. After the completion of our synthesis of pisiferic acid (**1**), the synthesis of both enantiomers of *O*-methylpisiferic acid was described by Japanese workers.[26]

Experimental

M.p.s were determined on a Kofler hot-stage and are uncorrected. Unless otherwise stated, i.r. spectra were taken on a Perkin-Elmer 337 spectrophotometer for KBr discs or liquid films and ^{1}H n.m.r. spectra, recorded on a Varian A-90 spectrometer, were measured in CCl_4 with TMS as internal standard. Mass spectra were recorded on Dupont 21-492B and Hitachi-Perkin-Elmer RMU-6H spectrometers at 70 eV using a direct-inlet system. Column chromatography was carried out with neutral Brockman alumina or silica gel (BDH). T.l.c. plates were coated with silica gel having a thickness of *ca.* 2 mm and the spots were located by exposing the dried plates to iodine vapour and u.v. light. Unless otherwise stated, all organic extracts were washed with brine, dried ($MgSO_4$), and evaporated under reduced pressure. Microanalyses were carried out in the Franz Pascher Microanalytiches Laboratorium at Bonn, Germany. All compounds described herein are racemic although the prefix (±) is omitted and only one enantiomer is depicted in the structural formula.

Dry solvents were distilled immediately before use. THF was distilled from lithium aluminium hydride. Ether was distilled from sodium metal.

Decahydro-4a,8,8-*trimethyl*-4β-(*tetrahydropyran*-2-*yloxy*)-*naphthalen*-1-*one* (**15**).—A solution of the pyranyl derivative (**14**) (3.31 g) in dry pyridine (20 ml) was added to the Sarett reagent[9] prepared from CrO_3 (4.12 g) and dry pyridine (40 ml) cooled to 0—5 °C. The mixture was left at room temperature for 20 h and then diluted with water and extracted with ether. The extract was washed, dried, and evaporated to give an oily material which on purification over a column of alumina (eluant hexane) afforded the *ketone* (**15**) (2.43 g, 74%), m.p. 89—91 °C (from hexane); *m/z* 210 ($M^+ - C_5H_8O$); $\nu_{max.}$(KBr) 1 710 cm^{-1} (C=O); δ_H 0.90 (3 H, s), 0.98 (3 H, s) and 1.20 (3 H, s, together 8-Me_2 and 4a-Me) (Found: C, 73.5; H, 10.3. $C_{18}H_{30}O_3$ requires C, 73.43; H, 10.27%).

Decahydro-4a,8,8-*trimethyl*-4β-(*tetrahydropyran*-2-*yloxy*)-*naphthalen*-1β-*ol* (**16**).—A mixture of the ketone (**15**) (3.01 g) and $LiAlH_4$ (0.51 g) in dry THF (190 ml) was heated under reflux for 10 h. To the mixture was added successively water (1 ml), sodium hydroxide (10%; 1 ml), and water (1 ml). The precipitate was filtered off, and the filtrate was evaporated under reduced pressure. The crude product was purified by column chromatography on silica gel using hexane–ether (1:3) to give the *alcohol* (**16**) (1.55 g, 56%), m.p. 112—113 °C (from ether); *m/z* 194 ($M^+ - C_5H_8O{\cdot}H_2O$); $\nu_{max.}$(KBr) 3 450 cm^{-1} (OH); δ_H 1.08 (3 H, s), 1.24 (3 H, s) and 1.28 (3 H, s together 8-Me_2 and 4a-Me), and 3.28—4.26 (4 H, m, 2′-, 1-, and 4-H) (Found: C, 73.0; H, 10.8. $C_{18}H_{32}O_3$ requires C, 72.92; H, 10.88%).

1β,4aβ-*Epoxydecahydro*-8,8-*dimethyl*-4β-(*tetrahydropyran*-2-*yloxy*)*naphthalene* (**20**) *and* 1β,8β-*Epoxydecahydro*-4a,8-*dimethyl*-4β-(*tetrahydropyran*-2-*yloxy*)*naphthalene* (**24**).—A mixture of $Pb(OAc)_4$ (6.71 g) and anhydrous $CaCO_3$ (6.71 g) was dried under reduced pressure and then heated and stirred with cyclohexane (100 ml) under reflux for 30 min. A solution of the alcohol (**16**) (1.52 g) in cyclohexane (30 ml) was then added to the suspension followed immediately by I_2 (1 g). The mixture was heated under reflux for 1 h with two Philips 500-W photolamps. The cooled mixture was filtered and the filter cake washed thoroughly with ether. The combined organic solvents were washed with 1% aqueous NaOH and the colour of the I_2 was removed by washing with aqueous $NaHSO_3$. Subsequent washing and evaporation under reduced pressure afforded an oily material which on purification over a column of alumina [eluant hexane–ether (1:1)] yielded the *cyclic ether* (**20**) (650 mg, 45%), m.p. 77—79 °C (from hexane–ether); *m/z* 210 (M^+ —

C_5H_8O); δ_H 0.86 (3 H, s), 0.96 (3 H, s, 8-Me_2), 3.38—4.26 (6 H, m, 2′-H, 4-H, 1-H, and 9-H), and 4.72 (1 H, m, 6′-H) (Found: C, 73.45; H, 10.3. $C_{18}H_{30}O_3$ requires C, 73.43; H, 10.27%).

Elution with hexane–ether (1:3) yielded the oily cyclic ether (**24**) (150 mg, 10%); *m/z* 210 ($M^+ - C_5H_8O$); δ_H 1.01 (3 H, s), 1.03 (3 H, s, 5- and 8a-Me), 3.42—4.32 (6 H, m, 2′-, 1-, 4-, and 11-H), and 4.78 (1 H, m, 6′-H) (Found: C, 73.5; H, 10.3. $C_{18}H_{30}O_3$ requires C, 73.43; H, 10.27%).

Decahydro-8,8-*dimethyl*-4-*oxonaphthalene*-1,4a-*carbolactone* (**21**).—A solution of chromium trioxide (0.19 g) in acetic acid (3 ml) was added to the cyclic ether (**20**) (0.29 g) dissolved in acetic acid (5 ml). The resulting deep brown solution was stirred at room temperature for 2 h, after which it was diluted with water and extracted with ether. That extract was washed, dried, and evaporated to give a syrup which on trituration with ether afforded the *lactone* (**21**) (170 mg, 80%), m.p. 80—81 °C (from ether); *m/z* 222 (M^+); $\nu_{max.}$(KBr) 1 765 (γ-lactone) and 1 712 cm^{-1} (CO); δ_H 0.91 (3 H, s) and 1.05 (3 H, s, 8-Me_2) (Found: C, 70.3; H, 8.2. $C_{13}H_{18}O_3$ requires C, 70.24; H, 8.16%).

Decahydro-4a,8-*dimethyl*-4-*oxonaphthalene*-1,4a-*carbolactone* (**25**).—A solution of chromium trioxide (80 mg) in acetic acid (3 ml) was added to the cyclic ether (**24**) (0.14 g) dissolved in acetic acid (3 ml). The resulting deep brown solution was stirred at room temperature for 2 h, after which it was diluted with water and extracted with ether. The extract was washed, dried, and evaporated to give a brown oil which, on trituration with ether, afforded the lactone (**25**) (80 mg, 78%), m.p. 119—121 °C (from ether) which remained undepressed on admixture with an authentic specimen and the i.r. spectrum of which was indistinguishable from that of the latter.

8aβ,4β-*Epoxydecahydro*-5,5-*dimethylnaphthalen*-1-*one* (**22**).—A solution of the cyclic ether (**20**) (550 mg) in acetone (5 ml) was cooled to 0 °C and treated with Jones chromic acid reagent (1 ml). The resulting solution was stirred at 0 °C, for 5 min and then treated with propan-2-ol to destroy the excess of oxidant, diluted with water, and extracted with ether. The extract was washed, dried, and evaporated, and the resulting oily material was chromatographed on alumina (hexane as eluant) to afford the *title compound* (**22**) (310 mg, 60%), m.p. 82—84 °C (from hexane); *m/z* 208 (M^+); $\nu_{max.}$(KBr) 1 710 cm^{-1} (C=O); δ_H 0.98 (3 H, s), 1.03 (3 H, s, 5-Me_2), and 3.85 (2 H, m, CH_2O) (Found: C, 74.9; H, 9.65. $C_{13}H_{20}O_2$ requires C, 74.96; H, 9.68%).

4β,9β-*Epoxydecahydro*-8,8-*dimethylphenanthren*-3-*one* (**27**).—Sodium hydride (60% dispersion in mineral oil) and dry methanol (0.09 ml) were added to a stirred solution of the keto ether (**22**) (520 mg) in freshly distilled ethyl formate (6 ml) cooled to 0 °C under nitrogen. The mixture was stirred at 0 °C for 30 min, after which dry ether (10 ml) was added and the resulting mixture stirred for 7 h at room temperature. Ice was added and the basic aqueous mixture was extracted with ether (3 × 15 ml). The combined extracts were washed with 5% aqueous sodium hydroxide. The alkaline washings were combined, cooled to 0 °C, and acidified with dilute hydrochloric acid. Nitrogen was bubbled into the acidic material during which time yellowish crystals appeared. The solid was filtered off and washed with water until the filtrate was no longer acidic to litmus paper. The material was dried *in vacuo* at 25 °C to yield the formyl derivative (**23**) (330 mg, 67%), m.p. 70—72 °C; *m/z* 236 (M^+); $\nu_{max.}$(KBr) 3 450 (OH) and 1 680 cm^{-1} (C=O). The formyl derivative (**27**) was found to be hygroscopic and unstable.

A solution of sodium methoxide [prepared from sodium (40 mg) in methanol (6 ml)] was added to a solution of the hydroxymethylene ketone (**23**) (320 mg) in dry methanol (7 ml), cooled in an ice-bath under nitrogen. A cold solution of 4-diethylaminobutan-2-one methiodide (920 mg) in methanol (5 ml) was added to the stirred mixture over 5 min. The resulting mixture was stirred for 20 h at room temperature, cooled, acidified with dilute hydrochloric acid (10%), and extracted several times with ether. The combined extracts were washed, dried, and evaporated to give dark oily material which on chromatographic purification over alumina (eluant benzene), produced the adduct (**26**) (285 mg, 71%), *m/z* 278 (M^+); $\nu_{max.}$(KBr) 1 710 cm^{-1} (CO); δ_H 2.06 (3 H, s) and 2.08 (3 H, s, MeCO for α- and β-epimer).

A solution of sodium methoxide [prepared from sodium (61 mg) and dry methanol (10 ml)] was slowly added under nitrogen to a solution of the adduct (**26**) (280 mg) in methanol (15 ml) cooled to 0 °C. The deep orange mixture was stirred at room temperature for 12 h, heated under reflux for 7 h, diluted with water, and extracted with ether. The extracts were washed, dried, and evaporated. Purification of the resulting residue over silica gel [eluant hexane–ether (8:2)] yielded the ketone (**27**) (190 mg, 70%), m.p. 108—110 °C (from hexane); *m/z* 260 (M^+); $\nu_{max.}$(KBr) 1 660 cm^{-1} (CO); δ_H 5.78 and 5.90 (2 H, m, 4-H). The ^1H n.m.r. spectrum was complicated owing to the mixture of epimers (Found: C, 78.45; H, 9.35. $C_{17}H_{24}O_2$ requires C, 78.42; H, 9.29%).

6β,20-*Epoxyabieta*-8,11,13-*trien*-12-*ol* (**31**).—A mixture of the ketone (**27**) (190 mg), diethyl carbonate (340 mg), sodium hydride (56% dispersion of sodium hydride in mineral oil; 37 mg) and 1,2-dimethoxyethane (2 ml) was heated in an oil-bath at 85 °C with stirring under nitrogen. After being heated at 85 °C for 2 h, the reaction mixture was cooled to 0—5 °C, acidified with acetic acid, diluted with water, and extracted with ether. The extract was washed, dried, and evaporated to give a yellow oil which on chromatographic purification over alumina (activity II) [eluant ether–hexane (1:9)] afforded the keto ester (**28**) (320 mg), *m/z* 332 (M^+ – EtOH); $\nu_{max.}$ 1 750 (ester CO) and 1 680 cm^{-1} (CO). The keto ester (**28**) was found to be unstable as shown by t.l.c.

A solution of the keto ester (310 mg) in ether (6 ml) was added, over a period of 5 min, to the stirred methyl-lithium solution (1.38M; 2 ml). The experiment was carried out under an argon atmosphere. The resulting solution was heated for 2 h, cooled, diluted with water, and extracted with ether. The extract was washed, dried, and evaporated to give a yellow oil which on purification over a column of alumina [eluant ether–hexane (2:8)] afforded the oily alcohol (**29**) (140 mg), $\nu_{max.}$ 3 340 (OH) and 1 665 cm^{-1} (CO).

The alcohol (**29**) (140 mg) was dissolved in methanol (5 ml) and then treated with hydrochloric acid (2 ml). The resulting red solution was heated under reflux for 8 h, diluted with water, and extracted with ether. The organic extract was washed, dried, and evaporated, and the residue chromatographed over silica gel [eluant hexane–ether (8:2)] to give the *title compound* (**31**) (100 mg, 46%), m.p. 102—104 °C (from ether); *m/z* 300 (M^+); $\nu_{max.}$(KBr) 3 360 cm^{-1} (OH); δ_H 0.95 (3 H, s), 1.03 (3 H, s together 2 × Me), 1.25 (6 H, d, *J* 7 Hz, $CHMe_2$), 3.86 (1 H, d, *J* 6 Hz), 3.98 (1 H, d, *J* 6 Hz), (20-H), and 6.62 (1 H, s) and 6.86 (1 H, s, together ArH) (Found: C, 80.00; H, 9.45. $C_{20}H_{28}O_2$ requires C, 79.95; H, 9.39%).

6β,20-*Epoxy*-12-*methoxyabieta*-8,11,13-*triene* (**32**).—Freshly distilled dimethyl sulphate (3 ml) and aqueous sodium hydroxide (3 ml, 10%) were added to a solution of the abietatrienol (**31**) (140 mg) in alcohol (30 ml, 95%). The reaction mixture was stirred at room temperature for 1 h and then heated at 80 °C for 1 h, after this it was diluted with water and extracted with ether. The extracts were washed, dried, and evaporated. Purification

of the resulting residue over alumina [eluant hexane–ether (9:1)] yielded the methoxylated compound (**32**) (90 mg, 60%); *m/z* 314 (M^+), δ_H 0.98 (3 H, s), 1.08 (3 H, s, together 2 × Me), 1.22 (6 H, d, *J* 7 Hz, $CHMe_2$), 3.85 (3 H, s, OMe), and 6.74 (1 H, s) and 7.01 (1 H, s, together ArH) (Found: C, 80.25; H, 9.65. $C_{21}H_{30}O_2$ requires C, 80.21; H, 9.62%).

Pisiferol (**2**).—Compound (**32**) (60 mg) dissolved in acetic acid (10 ml) was treated with powdered zinc (40 mg) and zinc iodide (40 mg) and heated under reflux for 6 h. The cooled reaction mixture was diluted with water and then filtered. The filtrate was extracted with ether several times. The extract was washed, dried, and evaporated to give pisiferol (**2**) (40 mg, 69%), m.p. 186—188 °C (from benzene; lit.,[4] 185—188 °C); *m/z* 302 (M^+); $\nu_{max.}$(KBr) 3 450br cm^{-1} (OH); δ_H 0.95 (3 H, s) and 0.99 (3 H, s, together 2 × Me), 1.18 (6 H, d, *J* 6 Hz, $CHMe_2$), 3.61 (1 H, d, *J* 10 Hz), 3.97 (1 H, d, *J* 10 Hz, CH_2OH), 6.10 (1 H, br s, 12-OH), and 6.63 (1 H, s) and 6.84 (1 H, s, together ArH) (Found: C, 79.5; H, 10.2. $C_{20}H_{30}O_2$ requires C, 79.42; H, 10.00%).

Methyl 12-*Methoxy*-7-*oxoabieta*-8,11,13-*trien*-20-*oate* (**9**).—Freshly distilled dimethyl sulphate (3 ml) and aqueous sodium hydroxide (2 ml, 10%) were added to a solution of pisiferol (**2**) (120 mg) in alcohol (25 ml; 95%). After being stirred at room temperature for 1 h, the reaction mixture was heated for 1 h at 80 °C, diluted with water, and extracted with ether. The extracts were washed, dried, and evaporated to give the methyl ester derivative (**8**) (138 mg), *m/z* 316 (M^+).

The crude oily product (**8**) (130 mg), completely free from the pisiferol (**2**) as shown by t.l.c., was dissolved in acetone (12 ml) and cooled to 0 °C. Jones reagent (3 ml) was added dropwise to the cooled solution and the resulting deep red solution was stirred at room temperature for 44 h. It was then treated with propan-2-ol to destroy the excess of oxidant, diluted with water, and extracted with chloroform. The extract was washed several times with aqueous sodium hydrogen carbonate. The alkaline extract was acidified with cold hydrochloric acid (2%) and extracted with chloroform. The extract was washed, dried, and evaporated to give acidic material which was esterified with diazomethane by the usual procedure. The material obtained on purification over a column of silica gel [hexane–ether (7:3)] afforded the title triene (**9**) (92 mg, 60%), m.p. 167—169 °C (from methanol) which proved to be identical with an authentic specimen[4] (mixed m.p. and i.r.) (Found: C, 73.85; H, 8.75. Calc. for $C_{22}H_{30}O_4$: C, 73.71; H, 8.44%).

Methyl 12-*Methoxyabieta*-8,11,13-*trien*-20-*oate* (**10**).—A mixture of the triene (**9**) (120 mg) and sodium borohydride (30 mg) in ethanol (3 ml) was stirred at room temperature for 4 h after which it was diluted with aqueous ammonium chloride and extracted with ether. The ether extract was washed, dried, and evaporated under reduced pressure. Toluene-*p*-sulphonyl chloride (210 mg) was added to the well-dried residue (130 mg) dissolved in pyridine (5 ml) and the mixture was stirred at room temperature for 20 h. It was then quenched with cold water and extracted with ether. The ether extract was washed, dried, and evaporated to give a thick oil. Sodium iodide (210 mg) and zinc dust (2 g) were added to the resulting tosyl derivative (150 mg) dissolved in 1,2-dimethoxyethane (10 ml) and the mixture was heated in an oil-bath at 100—120 °C for 2 h. The cooled reaction mixture was diluted with water and filtered and the filtrate was extracted with ether. The extract was washed, dried, and evaporated. Purification of the resulting material on silica gel (eluant benzene) afforded the title compound (95 mg, 82%), m.p. 110—112 °C (from methanol) which proved to be identical with an authentic specimen[4] (mixed m.p., and i.r.) (Found: C, 76.4; H, 9.4. Calc. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36%).

Pisiferic Acid (**1**).—*Method A*. A mixture of compound (**10**) (40 mg) and anhydrous aluminium bromide (310 mg) in ethanethiol (1.5 ml) was stirred at room temperature for 15 h. The mixture was poured into dilute hydrochloric acid and extracted, with ether. The extract was washed, dried, and evaporated and purification of the residue over silica [eluant ether–benzene (1:9)] afforded pisiferic acid (**1**) (32 mg, 90%), m.p. 226—227 °C (from ether–hexane and then sublimed) which proved to be identical with an authentic specimen (mixed m.p.); *m/z* 316 (M^+) and 271 ($M^+ - CO_2H$); $\nu_{max.}$(KBr) 3 490, 2 950—2 850 (OH), and 1 690 cm^{-1} (CO); δ_H 0.86 (3 H, s), 0.98 (3 H, s), 1.22 (6 H, d, *J* 7 Hz, $CHMe_2$), and 6.68 (1 H, s) and 6.82 (1 H, s, together ArH) (Found: C, 76.1; H, 9.1. Calc. for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92%).

Method B. A mixture of compound (**10**) (40 mg), freshly distilled quinoline (1 ml), and acetic acid (0.5 ml) was heated under reflux for 40 h under a slow stream of nitrogen. The mixture was poured into ether (10 ml) and the whole washed with 6M hydrochloric acid and then with aqueous sodium hydroxide (10%). The alkaline extract was acidified, extracted with chloroform, and the extract washed, dried, and evaporated to give acidic material (25 mg). To this dissolved in dichloromethane (2 ml) at −35 °C was added dropwise boron tribromide (0.6 ml) in dichloromethane (0.5 ml). The mixture was stirred for 10 min and allowed to reach room temperature. Work-up afforded dark red material which on chromatographic purification over silica gel [eluant ether–benzene (1:9)] afforded pisiferic acid (**1**) (22 mg, 62%) whose identity was confirmed by comparison with authentic material (mixed m.p., i.r., and t.l.c.).

Decahydro-1,1,4a-*trimethyl*-5β-(*tetrahydropyran*-2-*yloxy*) *naphthalen*-2-*one* (**18**).—A solution of the keto alcohol (**17**) (2.13 g) in dihydropyran (36 ml) containing toluene-*p*-sulphonic acid (77 mg) was stirred at room temperature for 35 min. Anhydrous potassium carbonate was added to the resulting solution and the mixture was then stirred for 2 min. After this it was diluted with water and extracted with ether. The extract was dried, washed, and evaporated to give an oil which on chromatographic purification over a column of alumina [eluant hexane–ether (9:1)] afforded the pyranyl derivative (**18**) (2.79 g, 93%). The product could not be distilled owing to its tendency to decompose; *m/z* 210 ($M^+ - C_5H_8O$); $\nu_{max.}$ 1 710 cm^{-1} (OH); δ_H 0.98 (3 H, s), 1.02 (3 H, s) and 1.06 (3 H, s, together 3 × Me), and 4.85 (1 H, t, *J* 6 Hz, 6′-H).

1,2,3,4,4a,5,8,8a-*Octahydro*-5,5,8a-*trimethylnaphthalen*-1β-*ol* (**33**).—A mixture of (**18**) (1.52 g) and sodium borohydride (810 mg) in ethanol was stirred at 0 °C for 1 h. The mixture was diluted with aqueous ammonium chloride and extracted with ether. The extract was washed, dried, and evaporated to give an alcohol (1.26 g), $\nu_{max.}$ 3 460 cm^{-1} (OH).

To the crude alcohol (1.25 g) dissolved in pyridine (5 ml) was added toluene-*p*-sulphonyl chloride (920 mg) and the mixture stirred at room temperature for 21 h. The resulting mixture was poured into ice–water and extracted with chloroform. The extract was washed, dried, and evaporated at room temperature to obtain the tosyl derivative (1.38 g), which being completely free from alcohol as evidenced by t.l.c., was used for the next step.

A mixture of the tosylate (1.25 g) and anhydrous lithium bromide (1.72 g) in dimethylformamide (10 ml) was heated in an oil-bath at 120—130 °C for 2 h. The cooled reaction mixture was diluted with water and extracted with ether. The extract was washed, dried, and evaporated to obtain an oily material which on chromatographic purification on silica gel [eluant hexane–ether (2:8)] afforded the *title alcohol* (**33**) [620 mg, 62% from (**18**)]; *m/z* 194 (M^+) and 176 ($M^+ - H_2O$); $\nu_{max.}$ 3 450 cm^{-1}

(OH); δ_H 0.98 (3 H, s), 1.05 (3 H, s), and 1.12 (3 H, s, together 3 × Me), and 5.65 and 5.72 (2 H, m, 6- and 7-H) (Found: C, 80.5; H, 11.5. $C_{13}H_{22}O$ requires C, 80.35; H, 11.41%).

3,4,4a,5,8,8a-*Hexahydro*-5,5,8a-*trimethylnaphthalen*-1(2H)-*one* (**34**).—Jones reagent (3 ml) was added to a solution of the alcohol (**33**) (520 mg) in acetone (10 ml) and the mixture stirred at 0 °C for 30 min. Isopropyl alcohol was added to destroy the excess of oxidant and this was followed by dilution with water and extraction with ether. The extract was washed, dried, and evaporated. Purification of the resulting residue over silica gel [eluant hexane–ether (9:1)] afforded the ketone (**34**) (480 mg, 93%); *m/z* 192 (M^+); $\nu_{max.}$ 1 725 cm^{-1} (CO); δ_H 1.02 (3 H, s), 1.12 (3 H, s), and 1.18 (3 H, s, together 3 × Me), and 5.65 and 5.78 (2 H, m, 6- and 7-H) (Found: C, 81.25; H, 10.55. $C_{13}H_{20}O$ requires C, 81.20; H, 10.48%).

1,2,4b,8a,9,10-*Hexahydro*-4b,8,8-*trimethylphenanthren*-3(2H)-*one* (**38**).—Sodium hydride (60% dispersion in mineral oil; 1.31 g) and dry methanol (1 ml) were added to a stirred solution of the ketone (**34**) (660 mg) in distilled ethyl formate (10 ml) cooled to 0 °C under nitrogen. The mixture was stirred at 0 °C for 25 min after which it was diluted with dry ether (20 ml) and stirred for 7 h at room temperature. Ice was added and the basic aqueous mixture was extracted (4 × 10 ml). The combined extracts were washed with 5% aqueous sodium hydroxide. The alkaline washings were combined, cooled to 0 °C, and acidified with dilute hydrochloric acid. Nitrogen was bubbled into the acidic material for 45 min during which time a reddish oil separated. It was taken up into ether and the solution washed until neutral to litmus, dried, and evaporated at room temperature to give the formyl derivative (**35**) (450 mg, 62%) as a dark semi-solid $\nu_{max.}$ 3 385 (OH), 1 660 (CO), and 1 590 cm^{-1} (C=C). The formyl derivative (**38**) was found to be very unstable and thus it was immediately used for the next step.

A solution of sodium methoxide [prepared from sodium (50 mg) in dry methanol (8 ml)] was added to a solution of compound (**35**) (420 mg) in dry methanol (10 ml) cooled in an ice-bath under nitrogen. A cold solution of 4-diethylamino-butan-2-one methiodide (6 g) in dry methanol (2 ml) was added dropwise to the stirred mixture over 5 min. The resulting mixture was stirred for 20 h at room temperature, cooled, acidified with dilute hydrochloric acid (10%), and extracted with ether. The extract was washed, dried, and evaporated to give an oil which on chromatographic purification over alumina (eluant benzene) produced the keto ester (**37**) (290 mg), *m/z* 262 (M^+) and 230 (M^+ − MeOH); $\nu_{max.}$(KBr) 1 710 cm^{-1} (CO); δ_H 2.06 (3 H, s) and 2.08 (3 H, s, MeCO for a α- and β-epimer). The keto ester (**37**) was found to be contaminated with two other products of weak intensity and could not be purified by chromatography. The product was directly subjected to cyclization.

Method A. A solution of sodium methoxide [prepared from sodium (61 mg) and dry methanol (10 ml)] was slowly added under nitrogen to a solution of the adduct (**37**) (250 mg) in methanol (15 ml) cooled to 0 °C. The deep orange mixture was stirred at room temperature for 2 h, heated under reflux for 7 h, and then diluted with water and extracted with ether. The extract was washed, dried, and evaporated to give a yellow oil which on chromatographic purification over silica gel [eluant hexane–ether (4:6)] afforded the tricyclic enone (**33**) [93 mg, 40% from (**39**)], *m/z* 244 (M^+); $\nu_{max.}$ 1 645 cm^{-1} (CO); δ_H 5.55—5.72 (m, 4-, 6-, and 7-H) (Found: C, 83.8; H, 10.18. $C_{17}H_{24}O$ requires C, 83.55; H, 9.90%).

Method B. A mixture of the adduct (**39**) (100 mg) and sodium hydride (42 mg) in anhydrous dimethoxyethane (15 ml) was heated at 70—85 °C for 3 h under argon. Some ice was added to the cooled mixture which was then passed through a column of silica gel with the aid of ethyl acetate. Removal of the solvent afforded a dense, dark oil which on chromatographic purification over silica gel afforded the tricyclic enone (**38**) [55 mg, 60% from (**37**)] whose identity was confirmed by comparing its spectral properties and t.l.c. behaviour with the specimen already prepared by method A.

12-*Methoxyabieta*-2,8,11,13-*tetraene* (**41**).—A mixture of the tricyclic enone (**38**) (160 mg), diethyl carbonate (340 mg), sodium hydride (56% dispersion of sodium hydride in mineral oil; 37 mg) and dimethoxyethane (2 ml) was heated on an oil-bath at 85 °C for 2 h. It was then cooled and quenched with absolute ethanol to destroy the excess of sodium hydride. A solution of aqueous acetic acid (5 ml) was added to the cold reaction mixture with rapid stirring under nitrogen and the mixture extracted with ether. The extract was washed with aqueous sodium hydrogen carbonate (5%) and brine, dried, and evaporated to give a yellow oil which was chromatographed over a column of neutral alumina (activity II) (eluant ether). This afforded the *keto ester* (**39**) (115 mg, 56%) as a deep yellow oil which was completely free from the tricyclic enone (**38**) as evidenced by t.l.c.; *m/z* 316 (M^+) and 270 ($M^+ - C_2H_5OH$); $\nu_{max.}$ 1 750 (CO) and 1 680 cm^{-1} (CO).*

A solution of the keto ester (**39**) (110 mg) in ether (6 ml) was added to stirred methyl-lithium in ether (1.38M; 2 ml) under argon. The ether solution was heated under reflux for 2 h after which it was cooled, and diluted with aqueous ammonium chloride (10%; 20 ml). The resulting solution was thoroughly extracted with ether, and the extract washed, dried, and evaporated to afford an alcohol (120 mg) [$\nu_{max.}$(KBr) 3 400 (OH) and 1 650 cm^{-1} (CO)] which was used directly in the next experiment.

The alcohol (120 mg) dissolved in methanolic hydrochloric acid (1%; 5 ml) was heated under reflux for 4 h, the progress of the reaction being monitored by t.l.c. The reaction mixture was diluted with water, extracted with ether, and the extract washed, dried, and evaporated to give a dark oil. Purification of this over silica gel [eluant hexane–ether (7:3)] afforded the abietatrienol (**40**) (52 mg); $\nu_{max.}$ 3 280 cm^{-1} (OH); δ_H 6.52 (1 H, s) and 6.62 (1 H, s, together 2 ArH).

Freshly distilled dimethyl sulphate (1 ml) and aqueous sodium hydroxide (10%; 1 ml) were added to a solution of the phenol (**40**) (50 mg) in alcohol (95%; 12 ml). The reaction mixture was stirred at room temperature for 1 h and then heated at 80 °C for 1 h. It was then diluted with water and extracted with ether. The extracts were washed, dried, and evaporated. Purification of the resulting product over alumina [eluant hexane–ether (9:1)] afforded the *title compound* (**41**) [57 mg, 56%, from (**38**)], *m/z* 298 (M^+); δ_H 0.98 (3 H, s), 1.08 (3 H, s), and 1.21—1.26 (9 H, 2 s, together 5 × Me) (since the methyl group signals were very close to each other the expected 14-Me doublet could not be measured), 3.75 (3 H, s, OMe), 5.52—5.56 (2 H, m, vinyl H), and 6.62 (1 H, s) and 6.68 (1 H, s, together 2 ArH) (Found: C, 84.65; H, 10.2. $C_{21}H_{30}O$ requires C, 84.51%; H, 10.13%).

12-*Methoxyabieta*-8,11,13-*trien*-2β-*ol* (**12**).—A solution of compound (**41**) (200 mg) in THF (5 ml) was added to a solution of diborane in THF at 0 °C, prepared by the addition of boron triflouride–ether (2 ml) to a suspension of sodium borohydride (620 mg) in THF (10 ml) under nitrogen. The mixture was stirred for 12 h at 0 °C and for 1 h at room temperature after

* Its ^1H n.m.r. spectrum was too complicated to interpret. In addition, during its purification it decomposed. Since distillation under high vacuum caused total decomposition the crude product was used directly for the next step.

which it was cooled to 0 °C and aqueous sodium hydroxide (10%; 6 ml) was cautiously added followed immediately by aqueous hydrogen peroxide (30%; 6 ml). The reaction mixture was heated under reflux for 1 h, cooled, and diluted with ether. The organic layer was separated, washed, dried, and evaporated to afford a gum which was passed over a column of alumina. Elution with benzene afforded the alcohol (**11**) (63 mg, 30%); *m/z* 316 (M^+) and 298 ($M^+ - H_2O$); $\nu_{max.}$ 3 460 cm^{-1} (OH).

A solution of the alcohol (**11**) (62 mg) in acetone (5 ml) was cooled to 0 °C and treated with Jones reagent (2 ml). The solution was stirred for 10 min at 0 °C and then treated with propan-2-ol to destroy the excess of oxidant, diluted with water, and extracted with ether. The extract was washed, dried, and evaporated to give a ketone (60 mg); $\nu_{max.}$ 1 710 cm^{-1} (CO).

The crude ketone (60 mg) dissolved in THF (5 ml) was added to lithium aluminium hydride (40 mg) in THF (15 ml) and the mixture heated for 4 h. It was then diluted with cold water and the resulting precipitate filtered off and the filtrate dried. Evaporation of the latter afforded a thick oil which was chromatographed over alumina. Elution with hexane–benzene (4:6) gave the alcohol (**12**) (38 mg, 63%) as a thick yellow liquid which failed to solidify; *m/z* 316 (M^+) and 298 ($M^+ - H_2O$); $\nu_{max.}$ 3 460 cm^{-1} (OH); δ_H 1.02 and 1.09 (each 3 H, s, 4-Me), 1.12 (6 H, d, *J* 8 Hz, $CHMe_2$), 1.18 (3 H, s, 10-Me), 3.76 (3 H, s, OMe), 4.26 (1 H, m. $W_{\frac{1}{2}}$ 16 Hz, 2-H), and 6.62 (1 H, s) and 6.86 (1 H, s, together 2 ArH) (Found: C, 79.9; H, 10.3. $C_{21}H_{32}O_2$ requires: C, 79.70; H, 10.19%).

2,20-*Epoxyabieta*-8,11,13-*triene* (**36**).—The alcohol (**12**) (40 mg) was added to a suspension of lead tetra-acetate (120 mg) and calcium carbonate (120 mg) in benzene (25 ml) and the mixture was heated under reflux with two Phillips 250-W photolamps for 2 h. The cooled reaction mixture was then filtered, and the filter cake washed thoroughly with benzene. The combined filtrates were washed with aqueous sodium hydrogen carbonate (2%) and brine, dried, and evaporated. Trituration of the resulting product with hexane–ether (9:1) afforded the title compound (**36**) (20 mg, 50%), m.p. and mixed m.p. 158—160 °C; *m/z* 314 (M^+); δ_H 1.01 (3 H, s) and 1.14 (3 H, s, together 2 × Me), 1.16 (6 H, d, *J* 7 Hz, $CHMe_2$), 3.74 (1 H, d, *J* 9 Hz), 4.28 (1 H, d, *J* 9 Hz, 20-H), 3.85 (3 H, s, OMe), and 6.65 (1 H, s) and 6.84 (1 H, s, together 2 ArH) (Found: C, 80.3; H, 9.7. $C_{21}H_{30}O_2$ requires C, 80.21%; H, 9.62%).

Acknowledgements

The authors thank Professor Takashi Matsumoto, University of Hiroshima, for providing the authentic specimens of the keto ester (**9**), pisiferic acid (**1**), and epoxyabietatriene (**36**), Professor S. C. Welch for donation of an authentic specimen of the lactone (**25**), and the Consejo Nacional de Investigaciones Cientificas y Tecnológicas (CONICIT) for partial financial support (Project SI-1973).

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Received 16th *March* 1987; *Paper* 7/476