# Influence of Electron Donating Aromatic Substituents on the Stereochemistry of the Products in Cycloalkylations of 2-(2-Arylethyl)-3,3-dimethyl-1-methylene-cyclohexane and Related Substrates: Mechanisms of Aromatic Cycloalkylations

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The critical role of the aromatic ring substituents in open chain substrates, in acid-catalysed aromatic cycloalkylations with an unsubstituted and a few isomeric mono- and di-methoxy substituted 2-(2-arylethyl)-3,3-dimethyl-1-methylenecyclohexanes 8a–d,h–j and two isomeric 2-(2-dimethoxy-phenylethyl)-1,3,3-trimethylcyclohexanols 5i,j, in determining the distributions of the respective trans- and cis-podocarpa-8,11,13-trienes, has been investigated and the results have been analysed. Olefin or alcohol precursors, having unactivated aromatic rings, proceed with high stereoselectivity via attack of the aromatic ring on a conformationally preferred cyclohexyl cation leading to the respective trans-products, while in substrates with an electron donating aromatic substituent para to the site of electrophilic attack, proceed directly in the exocyclic olefin or through the intervention of cyclohexenyl intermediates forming substantial amounts of the corresponding cis-products, in addition to the trans-products involving cyclohexyl cations.

Acid-catalysed aromatic cycloalkylation involving carbocations, e.g. 1 or the equivalent olefins 2, constitutes one of the simplest and most widely used methods for the synthesis of podocarpa-8,11,13-triene diterpenoids and various terpenoid

R = H, OMe, Me or Pr[i]
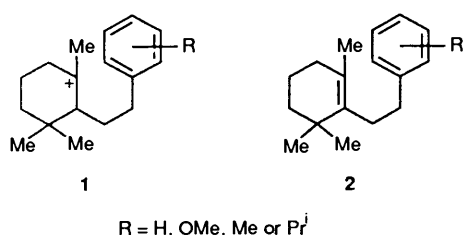
intermediates.[1-16] The stereochemistry and mechanisms of this [12,15,17,18] and the related cycloalkylation reactions leading to diterpenoid resin acids,[1,19-22] have been the subjects of intensive investigations for many years. Until recently, considerable confusion existed regarding the unpredictable stereochemical outcome of the cyclisation products, which seem to depend upon the 'reactivity'[18] of the aromatic rings in the open chain substrates. It has been demonstrated by Davis and co-workers,[23,24] and by us[25-28] that under mild conditions, using a MeSO_3H–P_2O_5 mixture as the reagent, the cyclisations of cyclohexanoles, having unactivated aromatic rings, e.g. 3a,b,[23,24] 4a,b,[23,24] and 5a,b,c,[25,26] proceed with high stereoselectivity leading to the respective trans-podocar-patrienes 6a,b,c in excellent yields. In contrast, under identical conditions the cycloalkylations of the substrates 3d,[24] 4d[24] and 5d–h,[26,27] incorporating an electron donating aromatic methoxy, methyl or isopropyl substituent para to the site of electrophilic attack, result in the corresponding trans- and cis-product mixtures 6d–h and 7d–h, along with other minor products. This apparent stereochemical dichotomy between the two series provided the key to our recently proposed[26,28] rational mechanisms, for the aromatic cycloalkylation reactions generating the trans- and cis-podocarpa-8,11,13-triene systems.

In order to gain deeper insights into an understanding the critical role of the 'reactivity' of the aromatic rings in the open chain substrates on the stereochemistry and mechanisms of aromatic cycloalkylation reactions, via a conformationally rigid carbocation and protonation–cyclisation process involving
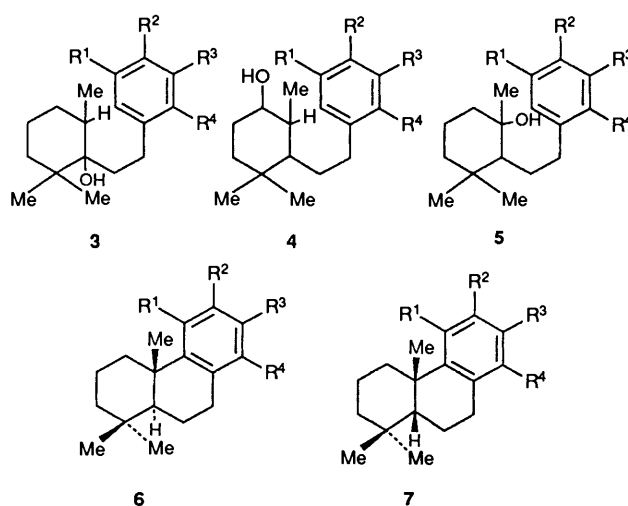

3a, 4a, 5a, 6a, 7a; R[1] = R[3] = R[4] = H; R[2] = OMe
3b, 4b, 5b, 6b, 7b; R[1] = R[2] = R[3] = H; R[4] = OMe
5c, 6c, 7c; R[1] = R[2] = R[3] = R[4] = H
3d, 4d, 5d, 6d, 7d; R[1] = R[2] = R[4] = H, R[3] = OMe
5e, 6e, 7e; R[1] = R[2] = R[4] = H; R[3] = Me
5f, 6f, 7f; R[1] = R[2] = R[4] = H; R[3] = Pr[i]
5g, 6g, 7g; R[1] = R[4] = H; R[2] = OMe; R[3] = Me
5h, 6h, 7h; R[1] = R[4] = H; R[2] = R[3] = OMe
5i, 6i, 7i; R[1] = R[4] = OMe; R[2] = R[3] = H
5j, 6j, 7j; R[1] = R[3] = H; R[2] = R[4] = OMe

cyclohexenyl intermediates[18] resulting in the respective trans- and cis-podocarpatrienes 6 and 7, we describe in this paper an extension of the cyclisation study on the unsubstituted and the mono- and di-methoxy aromatic ring substituted methylene cyclohexanes 8a–d,h–j and the isomeric dimethoxyphenylethyl-cyclohexanols 5i–j.

Results and Discussion

The easily accessible gem-dimethylcyclohexanones 9a–d,h[25,26] and 9i,j were smoothly transformed to the respective alkenes

8   9
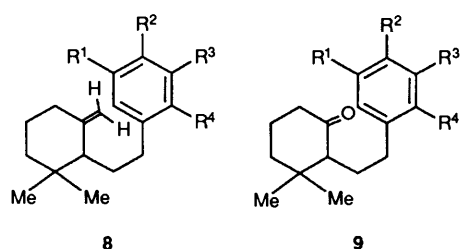
8a, 9a; $R^1 = R^3 = R^4 = H$; $R^2 = OMe$
8b, 9b; $R^1 = R^2 = R^3 = H$; $R^4 = OMe$
8c, 9c; $R^1 = R^2 = R^3 = R^4 = H$
8d, 9d; $R^1 = R^2 = R^4 = H$; $R^3 = OMe$
8h, 9h; $R^1 = R^4 = H$; $R^2 = R^3 = OMe$
8i, 9i; $R^1 = R^4 = OMe$; $R^2 = R^3 = H$
8j, 9j; $R^1 = R^3 = H$; $R^2 = R^4 = OMe$

11   12

13   10
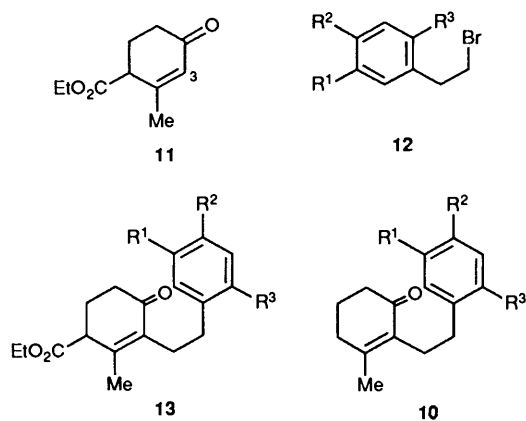
12i, 13i, 10i; $R^1 = R^3 = OMe$; $R^2 = H$
12j, 13j, 10j; $R^1 = H$; $R^2 = R^3 = OMe$

Table 1 Cyclisation of the cyclohexanols 5a–d,h–j and methylene-cyclohexanes 8a–d,h–j with $MeSO_3H$–P_2O_5. Ratio of trans- and cis-podocarpatrienes 6a–d,h–j and 7a–d,h–j

Entry	cyclohexanol/ olefin	Yield[a] (%)	products[b] trans + cis	ratio of trans/cis
1	5a[c]	93	6a + 7a	99:1[d]
2	8a	99	6a + 7a	100:0[f]
3	5b[g]	95	6b + 7b	100:0[f]
4	8b	99	6b + 7b	100:0[f]
5	5c[e]	93	6c + 7c	99:1[d]
6	8c	95	6c + 7c	99:1[d]
7	5d[g]	83	6d + 7d	42:58
8	8d	95	6d + 7d	34:66
9	5h[g]	82	6h + 7h	53:47
10	8h	95	6h + 7h	31:69
11	5i	90	6i + 7i	99:1[d]
12	8i	95	6i + 7i	99:1[d]
13	5j	92	6j + 7j	99:1[d]
14	8j	94	6j + 7j	99:1[d]

[a] Crude cyclised products after filtration through a short wide column of neutral alumina using light petroleum (60–80 °C) as solvent. [b] Products containing trans- and cis-isomers at least 75–99%. [c] Determined by GLC comparisons with authentic samples or integrated signal intensities of clearly separated peaks from ¹H NMR spectrum in $CDCl_3$ at 200 MHz and the detectable range of high field (0.3–0.4 ppm) signal of 4α-methyl group of cis-isomer is <1%. [d] Within or less than 1%. [e] Ref. 25. [f] Could not be detected in ¹H NMR. [g] Ref. 26.

8a–d,h–j by Wittig reaction under forcing conditions following the method described earlier[29] for the synthesis of 8a and 8c. The alcohols 5i and 5j were obtained as a single epimer, in each

case (stereochemistry not assigned), by condensation of the respective ketones 9i and 9j with MeMgI. The previously unknown cyclohexanones, 9i and 9j were prepared in good yields by our recently developed procedure[25,26] involving conjugate addition of a methyl group to the respective cyclohexenones 10i and 10j with an excess of $LiMe_2Cu$ in Et_2O at -30 to -25 °C in the presence of BF_3·Et_2O. The cyclohexenones 10i and 10j were obtained by alkylation[30] of Hagemann's ester 11 with the phenylethyl bromides 12i and 12j respectively, followed by alkaline hydrolytic decarboxylation of the corresponding C-3-alkylated products 13i and 13j.

The alcohols 5i,j and the olefins 8a–d,h–j were cyclised with $MeSO_3H$–P_2O_5, according to the conditions described earlier.[26] Quantitative evaluations of trans- and cis-cyclised products are outlined in Table 1, along with some of our relevant earlier reported results[25,26] from the substrates 5a–d,h for comparisons. The major trans-product from each of the cyclisation reaction was identified by GLC and ¹H NMR spectroscopic comparisons with authentic samples, in addition the cis-product was also specifically identified by the presence or absence of the[16] upfield signal (to the extent of <1%) of the C-4α-methyl group ($δ_H$ 0.3–0.4).

The cyclisation of the p-methoxy, o-methoxy and des-methoxy olefins 8a,8b and 8c gave the respective trans-products 6a,6b and 6c in excellent yields. However, the m-methoxy olefin 8d produced a mixture of the respective trans- and the cis-cyclised ethers 6d and 7d (Table 1).* It may be noted that the cyclisation of the m-methoxy alcohol 5d gave[26] a mixture of the trans- and the cis-products in a ratio of 42:58 in 83% yield along with three other minor components (ca. 17%). The cyclisation of the o-dimethoxy olefin 8h gave a mixture of the respective trans- and the cis-products 6h and 7h (Table 1). Careful chromatographic separation of this mixture gave the known trans-product 6h[26] and the pure cis-products 7h. Cyclisations of the isomeric dimethoxy olefins 8i and 8j or the corresponding alcohols 5i and 5j gave the virtually pure trans-products 6i[31] and 6j in excellent yields.

Our extensive results from the present and the earlier investigations[25,26] (Table 1) on the stereochemistry of cycloalkylation of the cyclohexanols 5a–d,h–j and the olefins 8a–d,h–j, particularly under mild condition using $MeSO_3H$–P_2O_5 as the reagent, provide with some important generalisations. These results are also consistent and qualitatively comparable with the observations of Davis and co-workers[23,24] on the cyclisations of the cyclohexanol substrates 3a,b,d and 4a,b,d. The cyclisations of the olefins 8a–c,i,j, with the unactivated aromatic nucleus, lead cleanly to the respective trans-products 6a–c,i,j, even in higher purity and yields compared to that from the respective cyclohexanols 5a–c,i,j. In contrast the cyclisations of the cyclohexanol substrates 5d,h[26] and the olefins 8d,h, that incorporate an electron donating methoxy substituent, para to the site of electrophilic attack on the aromatic ring, including the disubstituted aromatic precursors generate predominating or substantial amounts of the corresponding cis-isomers 7d,h, along with the trans-isomers 6d,h. It is important to note that the olefins 8d and 8h (Table 1, entries 8 and 10) gave more of the cis-products compared to that from the cyclisations of the respective cyclohexanols 5d and 5h (entries 7 and 9). It is clearly evident that it is the location of the electron donating aromatic substituent with respect to the site of electrophilic attack that governs the 'reactivity' of the aromatic ring in the open-chain substrates. The stereochemical results of the present and earlier works[23,24] of aromatic cycloalkylation reactions leading to the trans- and the cis-

* No cyclisation product corresponding to ortho-OMe could be detected.
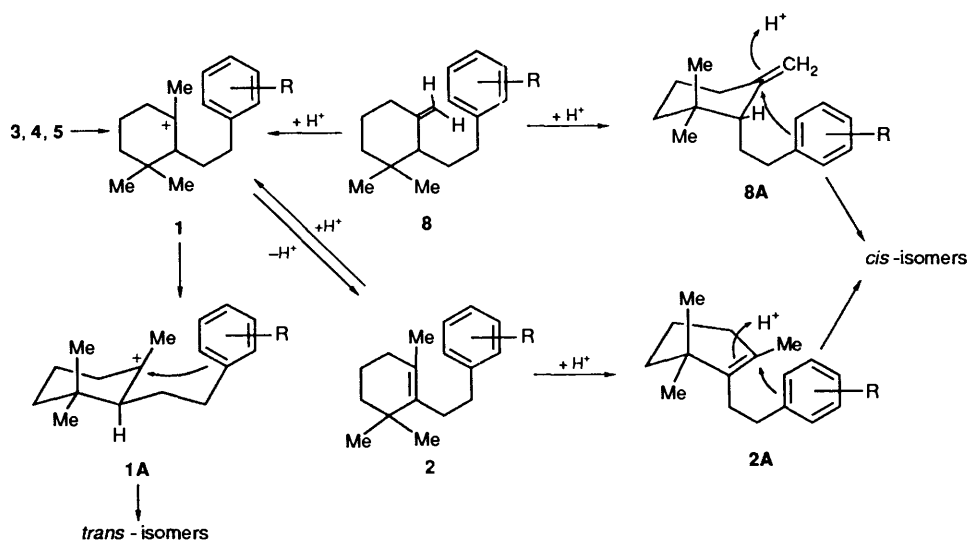
Scheme 1

podocarpa-8,11,13-trienes, can be explained by the consideration that aromatic rings without *para* activating group are not sufficiently nucleophilic to react through the concerted protonation cyclisation pathways,[18,32] *e.g.* **2A** or **8A** leading to the respective *cis*-products (Scheme 1), but require complete protonation to a carbocation, such as **1**, which reacts with high stereoselectivity by a pathway, *e.g.* **1A** due to minimum steric effects[18,22] to give *trans*-products. With an activating *para* aromatic substituent, the pathways **2A** or **8A** compete with pathway **1A** to give a mixture of the *cis*- and *trans*-products. The formation of a substantially higher proportion of the *cis*-products from the olefins **8d** and **8h**, compared to that from the corresponding alcohols **5d** and **5h** clearly indicates that the concerted cyclisation of the olefins through a path, such as **8A** is relatively faster than that of the protonation steps leading to the cations **1**.

In conclusion, the present study provided substantial evidences on the stereochemical results and rational mechanistic analyses for the first time, revealing the importance of the 'reactivity'[18] of the aromatic rings in the open chain substrates in cycloalkylation process leading to podocarpa-8,11,13-trienes, which should prove useful for prediction of the stereochemical outcome of other related cycloalkylation reactions leading to diterpenoid resin acids.[22,33,34]

Experimental

The compounds described are all racemates. M.p.s and b.p.s are not corrected. IR spectra of solids (KBr) and liquids (film) were recorded on a Perkin-Elmer model PE 298 instrument. ^{1}H NMR spectra were recorded at 200 MHz on an XL-200 spectrometer for solutions in $CDCl_3$ with $SiMe_4$ as internal standard, *J* values are given in Hz. Analytical GLC was performed on a Shimadzu GC-9A model with a flame-ionisation detector employing a 1.5% OV-17 (6.5 ft × 0.25 in) column with N_2 as the carrier gas. Column chromatography was performed on neutral alumina (Brockmann Grade 1, of BDH, India) or silica gel [Glaxo Laboratory (India) Ltd.]. Light petroleum refers to fractions of b.p. 40–60 °C unless otherwise stated. Ether refers to diethyl ether. Elemental analyses were performed by Mr. P. P. Bhattacharya and S. K. Sarkar of this laboratory.

Ethyl 3-[2-(2,5-*Dimethoxyphenyl*)*ethyl*]-2-*methyl*-4-*oxo-cyclohex*-2-*ene*-1-*carboxylate* **13i**.—Hagemann's ester **11** (8.37

g, 0.046 mol) was alkylated[30] with the bromide **12i**[32] (8.52 g, 0.04 mol) in the presence of Bu^tOK, prepared from potassium metal (1.56 g, 0.04 mol), in Bu^tOH to afford the desired alkylation product **13i** (9.57 g, 70%), b.p. 210–220 °C (0.2 mmHg) (Found: C, 69.0; H, 7.50. $C_{20}H_{26}O_5$ requires C, 69.34; H, 7.57%); v_{max}/cm^{-1} 1728 (ester) and 1670 (α,β-unsaturated ketone); δ 1.28 (3 H, t, *J* 7, CO_2CH_2Me), 1.86 (3 H, s, vinyl Me), 2.26–2.62 (8 H, m), 3.24 (1 H, br s, $CHCO_2Et$), 3.76 (3 H, s, ArOMe), 3.78 (3 H, s, ArOMe), 4.20 (2 H, q, *J* 7, CO_2CH_2Me) and 6.66–6.80 (3 H, m, ArH).

Ethyl 3-[2-(2,4-*Dimethoxyphenyl*)*ethyl*]-2-*methyl*-4-*oxo-cyclohex*-2-*ene*-1-*carboxylate* **13j**.—Hagemann's ester **11** (8.37 g, 0.046 mol) was alkylated[30] with the bromide **12j**[35] (8.52 g, 0.04 mol) in the presence of Bu^tOK, prepared from potassium metal (1.56 g, 0.04 mol), in Bu^tOH to afford the desired alkylation product **13j** (8.89 g, 65%), b.p. 200–210 °C (0.2 mmHg) (Found: C, 69.10; H, 7.87. $C_{20}H_{26}O_5$ requires C, 69.34; H, 7.57%); v_{max}/cm^{-1} 1730 (ester) and 1670 (α,β-unsaturated ketone); δ 1.28 (3 H, t, *J* 7, CO_2CH_2Me), 1.85 (3 H, s, vinyl Me), 2.08–2.59 (8 H, m), 3.26 (1 H, br s, $CHCO_2Et$), 3.80 (3 H, s, ArOMe), 3.82 (3 H, s, ArOMe), 4.21 (2 H, q, *J* 7, CO_2CH_2Me), 6.40–6.50 (2 H, m, 3- and 5-ArH) and 7.02 (1 H, d, *J* 8, 6-ArH).

2-[2-(2,5-Dimethoxyphenyl)ethyl]-3-*methylcyclohex*-2-*enone* **10i**.—Keto ester **13i** (8.90 g, 0.026 mol) was refluxed with a solution of KOH (8 g, 0.14 mol) in water (8 cm³) and EtOH (80 cm³) under N_2 for 14 h. The cooled reaction mixture was acidified with HCl (6 mol dm⁻³). The usual work-up[30] followed by distillation afforded the enone **10i** (5.25 g, 75%), b.p. 170 °C (0.2 mmHg), which solidified, m.p. 62 °C [from ether–light petroleum (60–80 °C)] (Found: C, 74.3; H, 7.75. $C_{17}H_{22}O_3$ requires C, 74.42; H, 8.08%); v_{max}/cm^{-1} 1665 (α,β-unsaturated ketone); δ 1.80 (3 H, s, vinyl Me), 1.94–2.60 (10 H, m), 3.77 (3 H, s, ArOMe), 3.81 (3 H, s, ArOMe) and 6.72–6.84 (3 H, m, ArH).

2-[2-(2,4-*Dimethoxyphenyl*)*ethyl*]-3-*methylcyclohex*-2-*enone* **10j**.—Keto ester **13j** (7.79 g, 0.022 mol) was converted, in the same way as described for **10i** into the α,β-unsaturated ketone **10j** which was obtained as an oil (4.29 g, 70%), b.p. 160–165 °C (0.2 mmHg) (Found: C, 74.1; H, 8.35. $C_{17}H_{22}O_3$ requires C, 74.42; H, 8.08%); v_{max}/cm^{-1} 1670 (α,β-unsaturated ketone); δ 1.71 (3 H, s, vinyl Me), 1.87–2.49 (10 H, m), 3.76 (3 H, s, ArOMe), 3.77 (3 H, s, ArOMe), 6.32–6.45 (2 H, m, 3- and 5-ArH) and 6.98 (1 H, d, *J* 8, 6-ArH).

2-[2-(2,5-*Dimethoxyphenyl*)*ethyl*]-3,3-*dimethylcyclo-hexanone* 9i.—This compound was prepared adopting a general procedure.[26] To a stirred suspension of CuI (11.4 g, 60 mmol) in dry ether (50 cm³) under N_2 at $-25\,°C$ was added[25] MeLi in ether (1.4 mol dm⁻³; 70 cm³, 98 mmol). The resulting yellow suspension was cooled to $-50\,°C$ and $BF_3·Et_2O$ (7.8 cm³, 63 mmol) was added. After 5 min the cyclohexenone 10i (5.4 g, 20 mmol) in ether (25 cm³) was added dropwise and the mixture stirred at $-30\,°C$ for 15 min. Additional $BF_3·Et_2O$ (7.8 cm³, 63 mmol) was added and stirring continued at $-30\,°C$ for 1 h. The mixture was allowed to warm to 0 °C and then quenched with aqueous NH_4Cl. Work-up, followed by chromatography (neutral alumina) afforded the cyclohexanone 9i (5.24 g, 90%) as an oil, b.p. 140–145 °C (0.2 mmHg) (Found: C, 74.3; H, 9.2. $C_{18}H_{26}O_3$ requires C, 74.44; H, 9.02%); v_{max}/cm^{-1} 1710 (CO); δ 0.76 (3 H, s, Me), 0.98 (3 H, s, Me), 1.55–2.62 (11 H, m), 3.80 (6 H, s, 2 × ArOMe) and 6.74–6.84 (3 H, m, ArH).

2-[2-(2,4-*Dimethoxyphenyl*)*ethyl*]-3,3-*dimethylcyclo-hexanone* 9j.—The α,β-unsaturated ketone 10j (5.48 g, 20 mmol) was converted, in the same way as described for 9i into the ketone 9j (5.13 g, 88%), b.p. 145–150 °C (0.2 mmHg) (Found: C, 74.15; H, 9.2. $C_{18}H_{26}O_3$ requires C, 74.44; H, 9.02%); v_{max}/cm^{-1} 1710 (CO); δ 0.78 (3 H, s, Me), 0.98 (3 H, s, Me), 1.54–2.60 (11 H, m), 3.81 (3 H, s, ArOMe), 3.82 (3 H, s, ArOMe), 6.42–6.50 (2 H, m, 3- and 5-ArH) and 7.06 (1 H, d, J 8, 6-ArH).

2-[2-(2,5-*Dimethoxyphenyl*)*ethyl*]-1,3,3-*trimethylcyclohexan-1-ol* 5i.—To a well stirred ice-cold solution of the ketone 9i (3.88 g, 13.4 mmol) in dry ether (30 cm³) and ethereal solution of MeMgI, prepared from Mg-turnings (1.1 g). MeI (2.8 cm³, 45 mmol) in dry ether (20 cm³), was added dropwise for 1 h. The mixture was stirred for an additional 1 h at 0–5 °C and finally refluxed for 2 h. The mixture was decomposed with ice-cold saturated aqueous NH_4Cl. Work-up followed by chromatography (neutral alumina) afforded the cyclohexanol 5i (3.6 g, 90%); v_{max}/cm^{-1} 3380br (OH); δ 0.90 (3 H, s, Me), 0.94 (3 H, s, Me), 0.96–2.90 (12 H, m), 1.24 (3 H, s, Me), 3.77 (3 H, s, ArOMe), 3.79 (3 H, s, ArOMe) and 6.70–6.84 (3 H, m, ArH). This was used for cyclisation without further characterisation.

2-[2-(2,4-*Dimethoxyphenyl*)*ethyl*]-1,3,3-*trimethylcyclohexan-1-ol* 5j.—The ketone 9j (3.88 g, 13.4 mmol) was converted, in the same way as described for 5i into the alcohol 5j which was obtained as a viscous liquid (3.76 g, 92%); v_{max}/cm^{-1} 3380br (OH); δ 0.91 (3 H, s, Me), 0.95 (3 H, s, Me), 1.04–1.72 (12 H, m), 1.25 (3 H, s, Me), 3.83 (3 H, s, ArOMe), 3.84 (3 H, s, ArOMe), 6.42–6.54 (2 H, m, 3- and 5-ArH) and 7.06 (1 H, d, J 8, 6-ArH). This was used for cyclisation without further characterisation.

2-[2-(2-*Methoxyphenyl*)*ethyl*]-3,3-*dimethyl*-1-*methylene-cyclohexane* 8b.—This compound was prepared by the same procedure as described for 8a. A suspension of methyl(triphenyl)-phosphonium iodide (19.2 g, 45 mmol) in toluene (2 cm³) and a toluene solution of freshly prepared sodium *tert*-pentoxide[29,36] (36 cm³ of 1 mol dm⁻³ solution) was stirred at room temperature (*ca.* 25 °C) for 20 min. The ketone 9b (3.9 g, 15 mmol) in toluene (5 cm³) was added dropwise, the mixture was refluxed for 2 h, quenched with saturated aqueous NH_4Cl and extracted with ether. The extract was washed with aqueous NH_4Cl and water and dried (Na_2SO_4). Evaporation yielded an oil which was immediately filtered through silica gel with ether–light petroleum (60–80 °C) (1:19). The eluent was evaporated to give an oil (3.75 g) which was dissolved in light petroleum (60–80 °C) (10 cm³). Methyl iodide (3 cm³) was added and the mixture set aside at room temperature for 1 h. The precipitated methyl(triphenyl)phosphonium iodide was filtered off and the

filtrate concentrated under reduced pressure to give the pure alkene 8b (3.5 g, 90%), b.p. 130–135 °C (0.1 mmHg) (Found: C, 83.9; H, 9.9. $C_{18}H_{26}O$ requires C, 83.66; H, 10.14%); v_{max}/cm^{-1} 1645 (C=C); δ 0.72 (3 H, s, Me), 0.97 (3 H, s, Me), 1.16–2.72 (11 H, m), 3.75 (3 H, s, ArOMe), 4.46 (1 H, d, J 3) and 4.49–4.62 (m, 1 H) (C=CH₂) and 6.59–7.16 (4 H, m, ArH).

2-[2-(3-*Methoxyphenyl*)*ethyl*]-3,3-*dimethyl*-1-*methylene-cyclohexane* 8d.—The ketone 9d (3.9 g, 15 mmol) was converted in the same way as described for 8b into the alkene 8d which was obtained as an oil (3.5 g, 90%), b.p. 135–140 °C (0.1 mmHg) (Found: C, 84.0; H, 9.85. $C_{18}H_{26}O$ requires C, 83.66; H, 10.14%); v_{max}/cm^{-1} 1640 (C=C); δ 0.74 (3 H, s, Me), 0.82 (3 H, s, Me), 1.0–2.48 (11 H, m), 3.72 (3 H, s, ArOMe), 4.52–4.78 (2 H, m) (C=CH₂), 6.64–6.78 (3 H, m, ArH) and 7.16 (1 H, t, J 8, 5-ArH).

2-[2-(3,4-*Dimethoxyphenyl*)*ethyl*]-3,3-*dimethyl*-1-*methylene-cyclohexane* 8h.—The ketone 9h (3.47 g, 11.7 mmol) was converted in the same way as described for 8b into the alkene 8h which was obtained as an oil (3.09 g, 90%), b.p. 145–150 °C (0.1 mmHg) (Found: C, 79.4; H, 9.55. $C_{19}H_{28}O_2$ requires C, 79.11; H, 9.78%); v_{max}/cm^{-1} 1645 (C=C); δ 0.80 (3 H, s, Me), 0.89 (3 H, s, Me), 1.13–2.68 (11 H, m), 3.69 (3 H, s, ArOMe), 3.74 (3 H, s, ArOMe), 4.62 (1 H, d, J 3) and 4.75 (1 H, br s) (C=CH₂) and 6.16–6.82 (3 H, m, ArH).

2-[2-(2,5-*Dimethoxyphenyl*)*ethyl*]-3,3-*dimethyl*-1-*methylene-cyclohexane* 8i.—The ketone 9i (3.77 g, 13 mmol) was converted in the same way as described for 8b into the alkene 8i which was obtained as an oil (3.35 g, 90%), b.p. 138–142 °C (0.1 mmHg) (Found: C, 79.4; H, 9.5. $C_{19}H_{28}O_2$ requires C, 79.11; H, 9.78%); v_{max}/cm^{-1} 1645 (C=C); δ 0.82 (3 H, s, Me), 0.94 (3 H, s, Me), 1.10–2.84 (11 H, m), 3.78 (3 H, s, ArOMe), 3.79 (3 H, s, ArOMe), 4.72 (1 H, d, J 3) and 4.88 (1 H, s) (C=CH₂) and 6.70–6.90 (3 H, m, ArH).

2-[2-(2,4-*Dimethoxyphenyl*)*ethyl*]-3,3-*dimethyl*-1-*methylene-cyclohexane* 8j.—The ketone 9j (3.07 g, 10.6 mmol) was converted into the same way as described for 8b into the alkene 8j which was obtained as an oil (2.73 g, 90%), b.p. 140–145 °C (0.1 mmHg) (Found: C, 79.4; H, 9.5. $C_{19}H_{28}O_2$ requires C, 79.11; H, 9.78%); v_{max}/cm^{-1} 1645 (C=C); δ 0.79 (3 H, s, Me), 0.91 (3 H, s, Me), 1.04–2.48 (11 H, m), 3.64 (3 H, s, ArOMe), 3.69 (3 H, s, ArOMe), 4.59 (1 H, d, J 3) and 4.75 (1 H, br s) (C=CH₂), 6.19 (1 H, d, J 8, 5-ArH), 6.27 (1 H, s, 3-ArH) and 6.86 (1 H, d, J 8, 6-ArH).

Cyclisation of 5i *to* 6i.—Cyclohexanol 5i (500 mg, 1.63 mmol) in dry ether (5 cm³) was added to the acid mixture [prepared from $MeSO_3H$ (23 cm³; 0.35 mol) and P_2O_5 (3.7 g) by stirring for 2 h at room temperature] at 20–25 °C for 15 min. After usual work-up, the residual oil was purified by filtration [in light petroleum (60–80 °C)] through a short packed neutral alumina column (10 g) to afford 6i (423 mg, 90%), m.p. 133 °C [from light petroleum (60–80 °C)] (lit.,[31] m.p. 133–134 °C); δ 0.93 (3 H, s, Me), 0.96 (3 H, s, Me), 1.10–3.10 (11 H, m), 1.33 (3 H, s, 10-Me), 3.77 (3 H, s, ArOMe), 3.79 (3 H, s, ArOMe), 6.62 (1 H, d, J 8, ArH) and 6.72 (1 H, d, J 8, ArH); m/z 288 (M⁺, 100%), 273 (26), 217 (44), 208 (32), 203 (51), 193 (57), 191 (63), 177 (64), 165 (47), 151 (50), 135 (44), 121 (49), 105 (32), 91 (53), 77 (54), 69 (38), 55 (38) and 41 (45.)

Cyclisation of 5j *to* (±)-12,14-*Dimethoxypodocarpa*-8,11,13-*triene* 6j.—The cyclohexanol 5j (500 mg, 1.63 mmol) was converted, in the same way as described for 5i into 6i which was obtained as an oil (433 mg, 92%), b.p. 140 °C (0.5 mmHg) (Found: C, 79.35; H, 9.5. $C_{19}H_{28}O_2$ requires C, 79.12; H, 9.79%);

δ 0.94 (3 H, s, Me), 0.96 (3 H, s, Me), 0.98–2.92 (11 H, m), 1.21 (3 H, s, 10-Me), 3.84 (6 H, s, 2 × ArOMe), 6.34 (1 H, br s, 11-ArH) and 6.51 (1 H, br s, 13-ArH).

Cyclisations of the olefins **8a–d** *and* **8h–j** *with* $MeSO_3H$–P_2O_5. *Cyclisation of* **8a** *to* **6a**.—Methylenecyclohexane **8a** (500 mg, 1.93 mmol) in dry ether (5 cm³) was added to the acid mixture [prepared from $MeSO_3H$ (23 cm³; 0.35 mol) and P_2O_5 (3.7 g) by stirring for 2 h at room temperature] at 20–25 °C for 15 min. After usual work-up,[26] the residual oil was purified by filtration [in light petroleum (60–80 °C)] through a short packed neutral alumina column (10 g) to afford **6a** (495 mg, 99%), identical (IR, ¹H NMR and GLC) with the authentic sample.[25]

Cyclisation of **8b** *to* **6b**. Cyclisation of **8b** (500 mg, 1.93 mmol) with $MeSO_3H$–P_2O_5 as described for **6a** gave **6b** (495 mg, 99%); m.p. 116 °C, identical (mixed m.p., IR, ¹H NMR and GLC) with the authentic sample, m.p. 116 °C.[26]

Cyclisation of **8c** *to* **6c**. Cyclisation of **8c** (500 mg, 2.45 mmol) with $MeSO_3H$–P_2O_5 as described for **6a** gave **6c** (475 mg, 95%); identical (IR, ¹H NMR and GLC) with the authentic sample.[25]

Cyclisation of **8d** *to* **6d** *and* **7d**. Cyclisation of **8d** (500 mg, 1.93 mmol) gave an oil (475 mg, 95%). GLC analyses of the product showed the presence of the *trans*- and *cis*-compounds **6d** and **7d** in the ratio of 34:66 (97%, by co-injection with the pure sample of the *trans*-compound **6d**[26] and the *cis*-compound **7d**[37]).

Cyclisation of **8h** *to* **6h** *and* **7h**. Cyclisation of **8h** (500 mg, 1.73 mmol) with $MeSO_3H$–P_2O_5 gave an oil (475 mg, 95%). GLC analyses of the product showed the presence of the *trans*- and *cis*-compounds **6h** and **7h** in the ratio of 31:69 (97%, by co-injection with the pure sample of the *trans*-compound **6h**[26] and the *cis*-compound **7h** described below). Chromatography of this mixture (100 mg) on activated neutral alumina (10 g) and elution with light petroleum gave pure *cis*-product **7h** (67 mg, 67%) as a glassy solid (Found: C, 78.9; H, 9.9. $C_{19}H_{28}O_2$ requires C. 79.12; H, 9.79%); δ 0.45 (3 H, s, 4α-Me), 0.98 (3 H, s, 4β-Me), 1.20 (3 H, s, 10-Me), 1.22–2.92 (11 H, m), 3.89 (3 H, s, ArOMe), 3.91 (3 H, s, ArOMe), 6.61 (1 H, s, 11-ArH) and 6.87 (1 H, s, 14-ArH).

Cyclisation of **8i** *to* **6i**. Cyclisation of **8i** (500 mg, 1.73 mmol) with $MeSO_3H$–P_2O_5 as described for **6a** gave **6i** (475 mg, 95%), m.p. 133 °C, identical (mixed m.p., IR, ¹H NMR and GLC) with the sample described above.

Cyclisation of **8j** *to* **6j**. Cyclisation of **8j** (500 mg, 1.73 mmol) with $MeSO_3H$–P_2O_5 as described for **6a** gave **6j** (470 mg, 94%), identical (IR, ¹H NMR and GLC) with the sample described above.

Acknowledgements

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