Fig. 8 Calculated dipole moment for ground state and TS at HF/6-31G(d).

Fig. 9 Dependence of calculated solvent effect on the nuclear magnetic shielding. H-HF, B=B3LYP.

The dimerization of 5,6-dimethoxy-indene

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The reaction of 5,6-dimethoxy-indanol with acids or with triphenylphosphine-carbon tetrachloride afforded several dimeric compounds; in the dimerisation of 5,6-dimethoxy-indene with $\text{SiO}_2\text{-AgNO}_3$ only a single dimer was obtained.

In previous work we have studied the dimerisation of precocene II (6,7-dimethoxychromene) (1) with Lewis acids.^{1,4} In this way several dimers were obtained such as 2 and 3. Continuing with this work we have carried out studies of the dimerization of 5,6-dimethoxy-indene (4), which are described herein.

Our first approach was the preparation of 4. For this purpose we used the same procedure utilized to obtain 1 from 6,7-dimethoxy-2,2-dimethylchroman-3-one.¹ Thus, reduction of 5 with lithium aluminum hydride and treatment of the alcohol 6 formed with 4M HCl gave 5,6-dimethoxy-indene (4) and the dimers 7 and 9-11. These results indicated that under the same conditions the dehydration of 6,7-dimethoxy-2,2-dimethylchroman-3-ol was easier than that of 6, and that the dimerization of the latter occurs more easily than that of the former.

Our second attempt to prepare 4 was carried out as follows: 5,6-dimethoxy-1-indanone (5) was reduced with lithium aluminum hydride to give dimethoxy-1-indanol* (6) and a small amount of the symmetrical dimer A (7). Chromatography on silica gel of the mixture increased the formation of 7. Treatment of the alcohol 6 with triphenylphosphine in carbon tetrachloride-pyridine gave 4 and dimer B (9).

On the other hand, when 5,6-dimethoxyindene (4) was treated with silica gel impregnated with silver nitrate, a Lewis acid, only the dimer 9 was obtained. The same reaction with precocene II had led to type 2 dimers, analogous to 9, and of type 3, which is formed by one electron transfer oxidation and coupling.¹

The structure of the symmetrical dimer A (7) was given on the basis of the following considerations: Its high resolution MS was in accordance with the formula $\text{C}_{22}\text{H}_{20}\text{O}_5$, and its ^1H NMR spectrum was very similar to that of the alcohol 6. Thus, H-4 resonates at δ 6.77 in both compounds, H-7 at δ 6.88 (6.95 in the alcohol) and one of the H-2 appears as a multiplet at δ 2.15 (1.96 in the alcohol 6). The other H-2 is at δ 2.49 (m) (2.51 in the alcohol). The geminal proton to the other function appears as a doublet of doublets at δ 5.12 with couplings of 9 and 5 Hz (δ 5.21, br s, in 6). Other signals observed in the spectrum were: H-3 at δ 2.79 (m) and 3.05 (m), H-4 at 6.77 and the methoxy groups at 3.86 and 3.87. ^1H NMR proof of the dimeric structure of this compound was provided by the observation in the HMBC spectrum of a two bonds correlation between H-1 and C-1. Structure 4 represents the *meso* and/or racemic forms.

Dimer B (9) showed in the HRMS spectrum the molecular ion at 352.1647 ($\text{C}_{22}\text{H}_{20}\text{O}_4$). This compound had been prepared by dehydration of 6 with thionyl chloride or oxalyl chloride and the erroneous structure 8 had been assigned.^{6,8} Later, this substance was obtained by treatment of the indanone 5 with aluminum trichloride and subsequent Clemmensen reduction. In these works^{9,10} the structure was corrected to 9, now confirmed herein by assignment of the ^1H and ^{13}C NMR spectra, using 2D NMR data (COSY, HSQC and HMBC).

The other two dimeric compounds, dimers C (10) and D (11), were isomers showing the molecular formula $\text{C}_{22}\text{H}_{20}\text{O}_5$, and having a similar ^1H NMR spectrum. To the more abundant of them the structure 10 was assigned on the following basis: The ^1H NMR spectrum showed four aromatic protons (singlets at δ 6.68, 6.78, 6.87 and 6.93) and four methoxy groups, which explained the existence of four oxygens of the five present in the molecule. The fifth oxygen must be part of a secondary alcohol group, because its geminal proton was observed as a triplet at δ 5.09 ($J = 6.4$ Hz). Irradiation of this hydrogen, using double resonance experiments, transformed a septet at δ 2.70 into a double doublet. Alternatively, irradiation of this second signal collapsed the first into a broad singlet, transformed two double doublets, resonating at δ 2.51 ($J = 15.5$ and 8 Hz) and 2.88 ($J = 15.5$ and 8.5 Hz), into two doublets ($J = 15.5$ Hz) and converted a double doublet at δ 3.60 into a triplet. This indicated a partial structure of the type $-\text{CHOH}-\text{CH}(\text{CH}_2)-\text{CH}_2-$. The corresponding carbon resonances of this group appear at δ 79.9 (C-3), 54.3 (C-2) and 32.6 (C-1), respectively. These data fixed the structure of one of the hydroxylated indane part of the molecule. Other non-aromatic carbons resonated at δ 46.5 (C-1'), 28.6 (C-2') and 31.4 (C-3'). The corresponding hydrogen resonances, assigned by double resonance experiments, were H-1' at δ 3.60 (dd, $J = 14$ and 6.3 Hz), H-2' at δ 1.81 (m) and 2.21 (m) and H-3' at δ 2.51 (dd, $J = 15.5$ and 8 Hz) and 2.88 (dd, $J = 15.5$ and 8.5 Hz), indicating the existence of a $-\text{CH}-\text{CH}_2-\text{CH}_2-$ group. Furthermore, the resonance parameters of the hydrogens at C-2' and C-3' were similar to those described for 6-(2',3'-dihydro-1'H-inden-1'-yl)-1'H-indene.¹⁰ Thus, the structure of this dimer was determined as the racemate 10 and confirmed by the study of its 2D NMR data.

The chemical shifts and forms of resonance of H-4, H-7 and H-3 in the second isomer 11 (dimer D), which also represents a racemate, were identical with those of 10, indicating a similar stereostructure for the 3 α -hydroxy-indane part in both molecules. Consequently these two isomers must be epimeric at C-1'.

In relation to the relative stereochemistry of dimer C (10) and dimer D (11), a *cis* relationship was assigned to H-2(β) and H-3(β), considering the coupling value ($J \sim 6.4$ Hz) observed in the ^1H NMR spectra of both compounds. The calculated coupling constants for the less energy conformers were 7.4 and 8.3 Hz for the *cis* and *trans* stereochemistry, respectively. Both dimers C (10) and D (11) were transformed into dimer B (9) over time.

New Zealand authors¹² have studied the dimerization of 3,7-dimethyl-1H-inden-4-ol with acids obtaining the three dimers 12-14, which in the acid medium are in an equilibrium mixture. These dimers are comparable to compounds 9-11 now obtained by us. On the other hand, dimers 13 and 14 have the same stereochemistry at C-2, C-3 and are epimeric at C-1'. The change of stereochemistry of the methyl over this carbon from 13(α) to 14(β) produced in the ^{13}C NMR spectrum shifts to lower field of C-1 (from δ 31.5 to 34.0) and at higher field of C-2 (from δ 58.8 to 56.1). These effects have now also been observed for the change of stereochemistry of H-1' of (10)(α) to (11)(β), from δ 32.6 to 35.2 at C-1 and from δ 54.3 to 50.3 at C-2, respectively. Thus, dimer C (10) and dimer D (11) should have the same stereochemistry at C-1' as 13 and 14, respectively.

Experimental

^1H NMR spectra were taken in CDCl_3 solutions at 200.13 and 500.13 MHz, with a Bruker AC-200 or a Bruker AMX2-500 spectrometer, respectively, and the ^{13}C NMR were run at 125.03 MHz in a Bruker AMX2-500. MS and HRMS were taken at 70 eV (probe) in a Micromass Autospec spectrometer. Dry column chromatography were made on silica gel Merck 0.02-0.063 mm. HPLC was carried out in a Beckman System Gold mod. 125. Molecular mechanics calculations were carried out with Hyperchem 7.0 and coupling constants were predicted with Chem X.

Reduction of 5,6-dimethoxy-1-indanone (5) and treatment with acid. A solution of 5 (200 mg) in dry THF (9 ml) was treated with lithium aluminum hydride (20 mg) at reflux for 2 h. The excess of reagent was decomposed by addition of a few ml of EtOAc. The mixture was stirred with HCl 4N (2.5 ml) at room temp for 3 h. The solution was diluted with water and extracted with EtOAc. The organic layer was washed with 5% NaOH, water and dried over Na_2SO_4 . The solvent was evaporated *in vacuo* to give a residue, which was chromatographed on silica gel with petroleum-EtOAc (2:3) to afford, after rechromatography, 5,6-dimethoxyindan-1-ol (6) (30 mg), dimer A (7) (26 mg), dimer B (9) (22 mg) and a mixture of dimers C (10) (6 mg) and D (11) (1.5 mg). These last compounds were separated by normal-phase HPLC using a 250 x 10 mm silica gel column (Beckman Ultrasphere 5 μm particle size), an isocratic system of *n*-hexane-EtOAc (3:2), and a flow rate of 3 ml/min.

Reduction of 5,6-dimethoxy-1-indanone (5). A solution of 5 (300 mg) in dry THF (9 ml) was treated with lithium aluminum hydride (60 mg) at reflux for 1 h. The excess of reagent was decomposed by addition of EtOAc, then the solution was diluted with water and extracted with EtOAc. Removal of the solvent *in vacuo* and

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chromatography of the residue (280 mg) in silica gel with petroleum-EtOAc (2:3) afforded the dimer 7 (40 mg) and 5,6-dimethoxyindan-1-ol (6) (185 mg).

Dehydration of 5,6-dimethoxy-1-indanol (6). The alcohol 6 (66 mg) dissolved in CCl_4 (12 ml) and pyridine (3 ml) was treated with triphenylphosphine (200 mg) and the mixture was refluxed by 4 h. Extraction in the usual way with EtOAc and chromatography of the residue in silica gel with petroleum-EtOAc gave 5,6-dimethoxyindeno (4) (35 mg) and the dimer B (9) (4 mg).

5,6-Dimethoxyindene (4). ^1H NMR (500 MHz): δ 3.27 (2H, s, H-1), 3.83 and 3.84 (each 3H, s, -OMe), 6.38 (1H, dt, $J = 5.5$ and 1.9 Hz, H-2), 6.72 (1H, dtd, $J = 5.5$, 1.9 and 0.5 Hz, H-3), 6.90 (1H, s, H-4), 7.01 (1H, s, H-7); EIMS m/z (rel. int.): 176 [$\text{M}]^+$ (100), 161 (21), 149 (73), 141 (10), 133 (7), 111 (11).

5,6-Dimethoxyindan-1-ol (6). [$\text{M}]^+$ at m/z 194.0939. $\text{C}_{11}\text{H}_{14}\text{O}_2$ requires 194.0943; ^1H NMR (500 MHz): δ 1.96 and 2.51 (each 1H, m, H-2), 2.78 and 3.02 (each 1H, m, H-3), 3.88 and 3.89 (each 3H, s, -OMe), 5.21 (1H, br s, H-1), 6.77 (1H, s, H-4), 6.95 (1H, s, H-7); EIMS m/z (rel. int.): 194 [$\text{M}]^+$ (50), 176 (100), 161 (48), 151 (10), 146 (6), 133 (20), 118 (14), 115 (20), 105 (17).

Dimer A (7) [$\text{M}]^+$ at m/z 370.1879. $\text{C}_{22}\text{H}_{26}\text{O}_2$ requires 370.1780; ^1H NMR (500 MHz): δ 2.15 and 2.49 (each 2H, m, H-2), 2.79 and 3.05 (each 2H, m, H-3), 3.86 and 3.87 (each 6H, s, -OMe), 5.12 (2H, dd, $J = 9$ and 5 Hz, H-1), 6.77 (2H, s, H-4) and 6.88 (2H, s, H-7); EIMS m/z (rel. int.): 370 [$\text{M}]^+$ (18), 194 (23), 177 (100), 161 (17), 146 (12), 133 (8), 115 (7).

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Dimer B [2-(2',3'-dihydro-5',6'-dimethoxy-1'-H-inden-1'-yl)-5,6-dimethoxy-1H-indene] (9). [$\text{M}]^+$ at m/z 352.1647. $\text{C}_{21}\text{H}_{24}\text{O}_4$ requires 352.1675; ^1H NMR (500 MHz): δ 2.07 and 2.48 (each 1H, m, H-2'), 2.88 and 2.99 (each 1H, m, H-3'), 3.26 and 3.30 (each 1H, d, $J = 22$ Hz, H-1), 3.81, 3.88, 3.89 and 3.90 (each 3H, s, -OMe), 4.26 (1H, t, $J = 7.6$ Hz, H-1'), 6.51 (1H, s, H-3), 6.66 (1H, s, H-7'), 6.82 (1H, s, H-4'), 6.89 (1H, s, H-4), 7.00 (1H, s, H-7); EIMS m/z (rel. int.): 352 [$\text{M}]^+$ (88), 337 (13), 321 (14), 306 (6), 208 (11), 192 (7), 177 (100), 161 (6), 146 (10).

Dimer C [2 α -(2',3'-dihydro-5',6'-dimethoxy-1'-H-inden-1 β -yl)-3 α -hydroxy-5,6-dimethoxy-1H-indene] (10). [$\text{M} - \text{H}_2\text{O}]^+$ at m/z 352.1684. $\text{C}_{21}\text{H}_{24}\text{O}_5$ requires 352.1675; ^1H NMR (500 MHz): δ 1.81 and 2.21 (each 1H, m, H-2'), 2.51 (1H, dd, $J = 15.5$ and 8 Hz, H-1), 2.70 (1H, sept, $J = 14$, 8 and 6 Hz, H-2), 2.82 (1H, quint, $J = 15.5$ and 8.5 Hz, H-3'), 2.88 (1H, dd, $J = 15.5$ and 8.5 Hz, H-1), 2.92 (1H, m, H-3'), 3.60 (1H, dd, $J = 14$ and 6.3 Hz, H-1'), 3.85, 3.86, 3.87 and 3.89 (each 3H, s, -OMe), 5.09 (1H, t, $J = 6.4$ Hz, H-3), 6.68 (1H, s, H-7), 6.78 (1H, s, H-4), 6.87 (1H, s, H-7'), 6.93 (1H, s, H-4); EIMS m/z (rel. int.): 370 [$\text{M}]^+$ (32), 352 (53), 337 (14), 321 (13), 306 (6), 192 (9), 177 (100), 161 (20), 146 (10), 133 (11), 115 (9).

Dimer D [2 α -(2',3'-dihydro-5',6'-dimethoxy-1'-H-inden-1 α -yl)-3 α -hydroxy-5,6-dimethoxy-1H-indene] (11). [$\text{M}]^+$ at m/z 370.1756. $\text{C}_{22}\text{H}_{26}\text{O}_4$ requires 370.1780; ^1H NMR (500 MHz): δ 1.99 and 2.33 (each 1H, m, H-2'), 2.48 (1H, m, H-2), 2.84 (1H, dd, $J = 15.3$ and 8.7 Hz, H-1), 2.86 (1H, quint, $J = 13$ and 8 Hz, H-3'), 2.93 (1H, dd, $J = 15.3$ and 7.5 Hz, H-1), 2.97 (1H, m, H-1, H-3'), 3.56 (1H, m, H-1'), 3.90, 3.91, 3.92 and 3.95 (each 3H, s, -OMe), 5.13 (1H, t, $J = 6.4$ Hz, H-3), 6.81 and 6.82 (each 1H, s, H-4' and H-7), 7.01 (1H, s, H-4), 7.25 (1H, s, H-7'); EIMS m/z (rel. int.): 370 [$\text{M}]^+$ (10), 352 (39), 337 (10), 321 (9), 192 (11), 177 (100), 161 (15), 146 (12), 141 (28), 111 (15).

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Table 1. ^{13}C NMR data (δ) of 4, 6 and 7

	C	4	6	7
1	39.1	76.8	81.7	
2	132.8	36.4	33.4	
3	131.7	29.7	30.0	
3a	137.6	135.2	135.6	
4	104.6	107.5	107.4	
5	148.2	149.7	149.6	
6	147.2	148.4	148.2	
7	108.0	107.4	107.7	
7a	136.1	136.6	135.0	
-OMe	56.1	56.0	55.9	
-OMe	56.2	56.0	56.0	

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Table 2. ^{13}C NMR data (δ) of 9-11

C	9	10	11	C	9	10	11
1	38.4	32.6	35.2	1'	47.3	46.5	44.8
2	151.6	54.3	50.3	2'	34.3	28.6	30.8
3	126.6	79.9	76.	3'	31.5	31.4	31.2
3a	135.4	136.2	136.8	3'a	137.5	135.9	135.4
4	104.1	106.7	107.5	4'	107.5	107.6	107.6
5	148.1 ^a	148.5	148.3 ^a	5'	148.1 ^a	148.1 ^b	148.2 ^a
6	146.5	148.0 ^b	148.0 ^c	6'	148.2 ^a	149.5	149.9
7	108.3	107.3	107.6	7'	107.7	107.0	108.6
7a	135.5	133.7	135.6	7'a	137.8	137.3	138.2
-OMe	55.9	55.7	55.9	-OMe	56.1	55.9	56.0
-OMe	56.0	55.7	55.9	-OMe	56.3	56.1	56.1

^{a, b, c} These values can be interchanged

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