Synthesis of 1-ethyl-2-methyl-3-aryldindanes.
Stereochemistry of five-membered ring formation

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Dedicated to Professors Edmundo Rúveda and Roberto Rossi
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Abstract
A natural dimer of asarone and several analogues were obtained by acid-catalysed cyclodimerisation of styrenes and by formal [3+2] cycloaddition. A study of the influence of the aromatic ring substitution pattern on the stereochemistry of the reactions was carried out.

Keywords: Indanes, cyclodimerisation, formal [3+2] cycloaddition, stereochemistry

Introduction
A great number of compounds with an indane-like structure are found in nature. To this group belong those produced by biopolymerization of oxystyrenes and oxystilbenes, which have important biological properties such as anti-bacterial activity against Staphylococcus oxford and Escherichia coli, anti-fungal activity and anti-tumour in vitro activity by interacting with DNA. Among these compounds, a phenylindane, a dimer of asarone, may be found. The asarone and its dimer were originally isolated from the essential oil of Accorus calamus which is known as insect growth regulator, fungicide, insecticide, sedative and hypothermic agent.

The structure of 4,5,7-trimethoxy-1-ethyl-2-methyl-3-(2,4,5-trimethoxyphenyl) indane was assigned to the natural dimer of asarone. There are four possible diastereomers for this structure, namely α, β, γ and δ (Fig.1).

NMR studies, later confirmed by X-rays analysis, allowed the γ configuration to be assigned to this natural dimer.
Dimerisation in mineral acid medium,\textsuperscript{8} with ethyl polyphosphate (EPP),\textsuperscript{9} or with silica-supported phosphotungstic or phosphomolybdic acid (TPA/S and MPA/S)\textsuperscript{10} of isohomogenol and isosafrole, produces mainly cyclodimers with $\alpha$ configuration, accompanied by the $\gamma$ stereoisomer in some cases as a minor product.

Such cyclodimer type may also be obtained by formal [3+2] cycloaddition of alcohol derived cation and alkene.\textsuperscript{11} By this pathway, dimer configuration proved to be preferably $\alpha$ and $\beta$, depending on the stereochemistry of the starting alkene. Unlike acid-catalysed dimerisation, this reaction renders dimers with dissimilar substituents in the aromatic rings. This is possible since formal [3+2] cycloaddition of alcohol and alkene is faster than alkene dimerisation. Our experience with this cycloaddition,\textsuperscript{12} shows that starting from benzhydrols and alkenes, the $\alpha$ diastereomer was preferably obtained, with the $\gamma$ diastereomer occasionally as the minor product.

The $\delta$ stereoisomer has only been obtained by means of stereodirected synthesis.\textsuperscript{13} It has been postulated that both, cyclodimerisation of styrenes in acid medium\textsuperscript{10} and formal [3+2] cycloaddition,\textsuperscript{11} possess a common cationic intermediate (Scheme 1).

\begin{center}
\textbf{Scheme 1}
\end{center}
The dimerisation of asarone using hydrogen chloride or trifluoroacetic acid leads to the \( \gamma \) configured cyclodimer.\(^{14}\)

In this work, different pathways are described to obtain the natural asarone cyclodimer 2 and it is studied how the substitution pattern, in the aromatic rings of precursors, determines the steric course of cyclodimerisation.

**Results and Discussion**

The asarone dimer was obtained by three different routes and the product compared with the natural dimer extracted from *Accorus calamus* (Scheme 2).

![Scheme 2](image)

All routes led to the \( \gamma \) stereoisomer as a racemic mixture and as the principal product. Its physical data coincided with those of the natural product, \( \gamma \)-1-ethyl-\( \tau \)-2-methyl-\( \epsilon \)-3-(2,4,5-trimethoxyphenyl)-4,5,7-trimethoxyindane; however, the yield of the reactions was variable.

The dimerisation of asarone catalysed by sulphuric acid 50% (30 min., 70°C) afforded 2, with 13% yield. The synthesis of the indane structure via formal \([3+2]\) cycloaddition\(^{11}\) from asarone and its derivative alcohol 3, catalysed by SnCl\(_4\) (30 min., 0°C) afforded 2, with 40% yield. The highest yield (62%) was obtained when asarone dimerisation was carried out with TPA/S and MPA/S, using chloroform as solvent (1h, reflux temperature). In this synthetic process a secondary product 4, 1-(2,4,5-trimethoxyphenyl)propane,\(^{15}\) was detected, whose formation may be explained by the “ionic hydrogenation” method.\(^{16}\)
An obvious question that arises is why asarone dimerisation, using diverse acid catalysts or formal [3+2] cycloaddition, leads to the \( \gamma \) configured indane, when these reactions generally result in the \( \alpha \) indane configuration. Quite likely, one of the causes of the end product stereochemistry is the aryl substitution pattern of the starting products. In order to confirm such influence, a series of indanes differently substituted in the aromatic rings was synthesised.

In a previous paper, we reported the dimerisation of isosafrole 5 using TPA/S or MPA/S as catalysts.\(^{10}\) In both cases the racemates \( \alpha \) (7) and \( \gamma \) (8) were obtained in a 3:1 ratio. When the reaction was carried out via formal [3+2] cycloaddition, using 5 and 1-(3,4-methylenedioxyphenyl)propanol 6, compounds 7 (\( \alpha \)-racemate) and 8 (\( \gamma \)-racemate) were obtained in a 7:1 ratio (Scheme 3).

The prevalence of \( \alpha \) stereochemistry was also observed when 3,4,5-trimethoxystyrene 9 was treated with TPA/S affording dimeric compound 10 (Scheme 4); In the \( ^{13} \)C-NMR spectra of crude reaction it is observed the presence of signals of aliphatic carbons which are coincident which those described for \( \gamma \) isomers.\(^{4,10}\) When 9 was treated with alcohol 11 in the presence of SnCl\(_4\) the same dimer 10 was obtained. In the crude reaction mixture the presence of another diastereomer was not detected.
Differently substituted dimers were obtained from asarone 1 and several alcohols, namely, 6, 11 and 13, using formal [3+2] cycloaddition (Scheme 5). The main compounds obtained were 12, 15, and 14 respectively, all with α configuration. However, when alcohol 3 was treated with 1-methoxy-4-[(1E)-1-propenyl]-benzene 16, indane 17 with γ configuration was obtained as the only product.

Scheme 5
When 16 was treated with alcohols 11 and 13, it rendered indanes 18 and 19, both with α configuration (Scheme 6).

From these results it was inferred that, in order to obtain the γ isomer, at least two methoxy groups are required in 2 and 5-positions in the starting alkene in cyclodimerisation reactions, or in the alcohol in the case of formal [3+2] cycloaddition.

![Scheme 6](image)

**Scheme 6**

**Determination of indane configuration by NMR spectroscopy**

To confirm structures and stereochemistry of synthesised indanes, chemical shifts of hydrogen and carbon atoms were unequivocally assigned by 2D-NMR experiments. Comparison of 1H-NMR spectra of indanes of assigned γ configuration (γ-diasarone 2, indane 17, γ-diisohomogenol and γ-diisosafrole) disclosed remarkable coincidences (Table 1), except for H-3 of 2 which is highly deshielded (4.27 ppm) and its chemical shift is similar to those of H-3 in β-diisohomogenol (4.27 ppm) and β-metanethole (4.28 ppm). 8

<table>
<thead>
<tr>
<th>Table 1. Chemical shifts in 1H-NMR spectra of aliphatic hydrogen atoms in γ indanes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dimers/δ (ppm)</td>
</tr>
<tr>
<td>γ-diasarone (2)</td>
</tr>
<tr>
<td>γ-indane (17)</td>
</tr>
<tr>
<td>γ-diisohomogenol</td>
</tr>
<tr>
<td>γ-diisosafrole</td>
</tr>
</tbody>
</table>

Table 2 summarises 1H-NMR data of aliphatic hydrogen atoms of indanes of assigned α configuration.

Chemical shifts of aliphatic hydrogen atoms in indanes 10, 12, 14, 15, 18 and 19 are very
similar exception made for H-3 in compounds 12, 14 and 15 that were markedly deshielded, probably due to the methoxyl group in ortho position of the aryl ring at C-3.

Table 2. Chemical shifts in $^1$H-NMR spectra of aliphatic hydrogen atoms in α indanes

<table>
<thead>
<tr>
<th>Dimers/ δ(ppm)</th>
<th>H-1</th>
<th>H-2</th>
<th>H-3</th>
<th>CH$_3$</th>
<th>CH$_2$CH$_3$</th>
<th>CH$_3$CH$_3$</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>3.00</td>
<td>2.46</td>
<td>3.90</td>
<td>1.01</td>
<td>1.58</td>
<td>0.95</td>
</tr>
<tr>
<td>12</td>
<td>2.90</td>
<td>2.51</td>
<td>4.31</td>
<td>1.03</td>
<td>1.49/1.69</td>
<td>0.99</td>
</tr>
<tr>
<td>14</td>
<td>2.91</td>
<td>2.43</td>
<td>4.33</td>
<td>1.02</td>
<td>1.55/1.75</td>
<td>0.96</td>
</tr>
<tr>
<td>15</td>
<td>2.93</td>
<td>2.36</td>
<td>4.33</td>
<td>0.97</td>
<td>1.54/1.73</td>
<td>0.95</td>
</tr>
<tr>
<td>18</td>
<td>3.04</td>
<td>2.47</td>
<td>3.95</td>
<td>1.02</td>
<td>1.62</td>
<td>0.98</td>
</tr>
<tr>
<td>19</td>
<td>2.95</td>
<td>2.47</td>
<td>3.84</td>
<td>1.06</td>
<td>1.42/1.73</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Inter-proton coupling constants of hydrogen atoms in the five-member ring of several indanes of α, β and γ configuration are listed in Table 3. A quick inspection of Figure 1 shows that β- and γ-isomers have protons H-1 and H-3 in the same arrangement, cis and trans respectively, relative to H-2. This should lead to a high similarity in the observed $J_{1,2}$ and $J_{2,3}$ couplings for the compounds in β- and γ-configurations. In contrast, the α-isomers, with H-1 and H-3 in opposite arrangement with respect to H-2, should display dissimilar $J_{1,2}$ and $J_{2,3}$ couplings. These facts are punctually observed in Table 3. A detailed conformational analysis is performed below to explain the particular couplings displayed by 14 and 15, within α-isomers, and 2 and 17 within γ-ones.

Table 3. Coupling constants of aliphatic hydrogen atoms in α, β and γ indanes

<table>
<thead>
<tr>
<th>Dimers/ J (Hz)</th>
<th>$J_{1,2}$</th>
<th>$J_{2,3}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>α-diisohomogenol</td>
<td>7.2</td>
<td>9.5</td>
</tr>
<tr>
<td>α-diisosafrole</td>
<td>7.1</td>
<td>9.4</td>
</tr>
<tr>
<td>12 (α)</td>
<td>6.8</td>
<td>8.4</td>
</tr>
<tr>
<td>14 (α)</td>
<td>6.9</td>
<td>7.9</td>
</tr>
<tr>
<td>15 (α)</td>
<td>7.2</td>
<td>3.6</td>
</tr>
<tr>
<td>18 (α)</td>
<td>7.1</td>
<td>5.1</td>
</tr>
<tr>
<td>19 (α)</td>
<td>7.1</td>
<td>9.1</td>
</tr>
<tr>
<td>β-diisohomogenol</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>β-metanethole</td>
<td>7.0</td>
<td>7.0</td>
</tr>
<tr>
<td>γ-diisosafrole</td>
<td>9.5</td>
<td>9.0</td>
</tr>
<tr>
<td>γ-diasarone (2)</td>
<td>4.2</td>
<td>4.3</td>
</tr>
<tr>
<td>17 (γ)</td>
<td>5.5</td>
<td>5.3</td>
</tr>
</tbody>
</table>
The chemical shifts of $^{13}$C-NMR spectra of the $\alpha$, $\beta$ and $\gamma$ diatereomeric indanes are summarised in Table 4.

The comparison of the shifts of aliphatic carbon atoms in $\alpha$-diisohomogenol, $\alpha$-diisosafrole (7) and $\alpha$ diastereomers 10, 12, 14, 15, 18 and 19, revealed marked coincidences in the aliphatic carbons except for C-3 in the case of indanes 12, 14 and 15. The latter three indanes are significant for presenting the aryl group bound to C-3, with the same substitution pattern found in asarone.

In the case of $\gamma$ configured indanes 2 and 17, their similarity is also noteworthy, though the deshielding presented by the methyl group bound to C-2 and by the ethyl group methylene bound to C-1, with regard to the other diastereomers, should be highlighted. These values concur with an all trans arrangement of the substituents because the shielding $\gamma$ gauche trans effect, is smaller than the cis. Due to this $\gamma$ gauche trans effect, a greater deshielding is observed when the methyl group is in the trans arrangement with the substituent on C-1 and C-3. All these observations agree with the $\gamma$ configuration, which was originally assigned to the natural indane 2, and confirm the stereochemistry of compound 17 as well, making the $^{13}$C-NMR spectrum a useful tool for the configuration assignment of these compounds.

**Table 4.** $^{13}$C-NMR: chemical shifts of aliphatic carbon atoms in several indanes

<table>
<thead>
<tr>
<th>Dimers/δ (ppm)</th>
<th>C-1</th>
<th>C-2</th>
<th>C-3</th>
<th>CH₃</th>
<th>CH₂CH₃</th>
<th>CH₂CH₃</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\alpha$-diisohomogenol</td>
<td>48.3</td>
<td>49.3</td>
<td>56.7</td>
<td>13.6</td>
<td>22.2</td>
<td>12.0</td>
</tr>
<tr>
<td>$\alpha$-diisosafrole</td>
<td>48.3</td>
<td>49.4</td>
<td>56.7</td>
<td>13.7</td>
<td>22.0</td>
<td>12.1</td>
</tr>
<tr>
<td>7 (α)</td>
<td>48.3</td>
<td>49.4</td>
<td>56.7</td>
<td>13.6</td>
<td>22.2</td>
<td>12.0</td>
</tr>
<tr>
<td>10 (α)</td>
<td>48.7</td>
<td>48.9</td>
<td>56.6</td>
<td>15.4</td>
<td>22.5</td>
<td>12.9</td>
</tr>
<tr>
<td>12 (α)</td>
<td>48.7</td>
<td>48.8</td>
<td>49.0</td>
<td>14.6</td>
<td>22.6</td>
<td>12.8</td>
</tr>
<tr>
<td>14 (α)</td>
<td>48.9</td>
<td>49.0</td>
<td>49.5</td>
<td>14.7</td>
<td>22.7</td>
<td>12.9</td>
</tr>
<tr>
<td>15 (α)</td>
<td>48.5</td>
<td>48.2</td>
<td>46.6</td>
<td>15.3</td>
<td>22.0</td>
<td>12.9</td>
</tr>
<tr>
<td>18 (α)</td>
<td>48.7</td>
<td>48.4</td>
<td>55.4</td>
<td>15.2</td>
<td>22.5</td>
<td>12.9</td>
</tr>
</tbody>
</table>

**Conformational analysis**

The considerable difference in coupling constants of the $\gamma$ dimer of asarone 2 and 17 and the deshielding of H-3, in relation to other styrene dimers with $\gamma$ configuration, may be explained by taking into account extreme conformations for each indane. Using computational calculation tools and employing the semi-empirical method AM1, conformational analysis indicated that the most stable conformer for compounds 2 and 17 is that possessing the substituents in an all pseudoaxial arrangement, i.e., conformation $\gamma$-b, where H-1 and H-3 are in a gauche arrangement relative to H-2 and should display similar small $J_{1,2}$ and $J_{2,3}$ couplings, in accordance with our observations (cf. Table 3).
Calculations predict for 2 and 17 that the 1,3 interaction in the γ-b conformer between pseudoaxial substituents on C-1 and C-3 is lower than that in conformation γ-a, between such substituents in pseudoequatorial position and the methoxyl groups placed on C-4 and C-7 of the indane (Fig. 4). This is due to the presence of the substituent at the ortho position of the aromatic ring at C-3.

The rest of dimers in γ configuration, lacking the aforementioned substituent, are predicted to prefer the all-pseudoequatorial conformation γ-a, where H-1 and H-3 are in an anti arrangement relative to H-2 and should display also similar but high J_{1,2} and J_{2,3} couplings, in agreement with the experimental values (Table 3).

Dimers 12 and 19, of α configuration, are predicted to be in α-a as the preferred conformation (Figure 5). The expectation of J_{2,3} (anti) being higher that J_{1,2} (gauche) is observed in Table 3. Isosafrole and isohomogenol dimers with the same configuration behave likewise. Instead, J_{1,2}>J_{2,3} in indanes 10, 15 and 18 suggest a preference for the α-b conformation, probably due to the presence of the methoxyl group bound to the C-4 of the indane skeleton (Fig. 5). Finally, the similar coupling constants of compound 14 suggest there is no conformational preference in this case.
Origin of stereocontrol

While in isosafrole and isohomogenol dimerisations catalysed by sulphuric acid,\textsuperscript{9} EPP\textsuperscript{9} or heteropolyacids,\textsuperscript{10} the compound mainly obtained is the one with the \( \alpha \) configuration, in the case of asarone and indane 17 the only dimeric product afforded is the \( \gamma \) compound. This divergence could be interpreted by studying the possible structures of transition states by AM1 calculations. For isosafrole and isohomogenol, a type I\( \alpha \) approach (Figure 6) offers the advantage of minimising non-bonding interactions and allowing a certain degree of \( \pi \) stacking interaction between aromatic rings. This approach could lead to the I\( \beta \) intermediate, which via intramolecular cyclisation would afford the \( \alpha \)-configured isomer.

In the dimerisation of asarone and in the synthesis of 17, the presence of methoxyl groups in both ortho positions in the aromatic indane ring could destabilise I\( \alpha \) on steric grounds, thus making the type II\( \alpha \) approach (Figure 7) the most probable one, which in turn would generate intermediate II\( \beta \). Subsequent carbon-carbon bond rotation and cyclisation (II\( \gamma \)), would lead the pentagonal ring with the observed all trans substitution pattern.
Experimental Section

General Procedures. The $^1$H- and $^{13}$C-NMR spectra were recorded with a Bruker AC-300 spectrometer with CDCl$_3$ as solvent, employing Me$_4$Si as internal standard ($\delta$: 0.00), $J$ values are given in Hz. 2D-NMR experiments were recorded on a Bruker AC-500 instrument by using standard Bruker software. Melting point (uncorrected) was obtained with a Thomas Hoover apparatus. Preparative thin layer chromatography (p-tlc) was performed on a 20x20 cm glass plate coated with silica gel 60 F$_{254}$ (0.50 mm). Elemental analyses were carried out in our laboratories with a Coleman Analyser.

Cyclodimerisation of asarone with TPA/S or MPA/S. A mixture of asarone (0.104 g, 0.5 mmol) in chloroform (3 mL) and catalyst (0.05 meq; TPA/S: 100 mg, MPA/S: 50 mg) was heated at reflux during 1 h. After completion of reaction, monitoring by tlc, the catalyst was removed by filtration and the solvent evaporated under reduced pressure. The residue was purified via p-tlc using chloroform as solvent of elution yielding 2 (50%) as a solid; mp: 84-5 ° C, lit$^4$: 84 ° C.

Cyclodimerisation of asarone with sulphuric acid. A mixture of asarone (100 mg, 0.476 mmol) in water (30 mL) and concd. sulphuric acid (30 mL) was stirred for 30 minutes at 70 ° C: Then water (30 mL) was added and the crude product was extracted with chloroform (3x20mL). The organic layer was washed with aqueous solution of NaOH (5%) and water, dried over anhydrous Na$_2$SO$_4$ and the solvent was evaporated in vacuo. The compound 2 was purified by p-tlc using chloroform as solvent of elution; mp: 84-5 ° C, lit$^4$: 84 ° C. Yield: 13%.

Dimer of asarone by a formal cycloaddition [3+2] reaction. To a solution of 1-(2,4,5-trimethoxyphenyl)ethanol 3 (0.104 g, 0.464 mmol) and asarone (0.125g, 0.742 mmol) in dry Cl$_2$CH$_2$ (10mL) at 0°C, was added, with stirring, SnCl$_4$ (0.07 mL, 0.60 mmol). After 30 minutes the temperature was raised at room temperature and a NaCO$_3$H 5% solution (10 mL) was incorporated. The organic layer was separated, washed with water, dried over anhydrous Na$_2$SO$_4$ and the solvent was evaporated in vacuo. Purification of the residue by p-tlc using chloroform as
solvent of elution afforded product 2; mp: 84-5° C, lit\(^4\): 84° C. Yield 40%.

**1-(2,4,5-Trimethoxyphenyl)propan-1-ol (3).**\(^{18}\) Ethyl magnesium bromide (7.0 mmol in THF 5 mL) was added dropwise to a stirred solution of 2,4,5-trimethoxybenzaldehyde (5 mL, 3.28 mmol) at room temperature. The solution was stirred for 2h. Aqueous work up (H\(_2\)O, NH\(_4\)OH, ether) afforded 3 as white solid, mp: 68-70° Cº (0.510 g , 71%).

NMR data: \(\delta_H\): 0.93 (3H, t, J: 7.0 Hz, CH\(_3\)), 1.76 (2H, m, CH\(_2\)), 2.39 (1H, s, OH), 3.81 (3H, s, OCH\(_3\)), 3.83 (3H, s, OCH\(_3\)), 3.87 (3H, s, OCH\(_3\)), 4.77 (1H, dd, J: 5.1 and 8.9 Hz, CH), 6.51 (1H, s, Ar), 6.87 (1H, s, Ar). \(\delta_C\): 10.4, 30.4, 56.2 (2), 56.6, 71.5, 97.6, 111.1, 124.2, 143.1, 148.6, 150.7.

**1-(3,4-Methylenedioxyphenyl)propan-1-ol (6).**\(^{19}\) The same procedure described for the preparation of 3 was carried out with ethylmagnesium bromide (28 mmol in 14 mL of THF) and piperonal (13.1 mmol in 2 mL of THF) afforded 6 as clear oil (1.6 g , 68%).

NMR data: \(\delta_H\): 0.90 (3H, t, J: 7.4 Hz, CH\(_3\)), 1.70 (1H, m, J: 6.3, 7.4 and 14.7 Hz, CH\(_2\)), 1.79 (1H, m, J: 6.3, 7.4 and 14.7 Hz, CH\(_2\)), 1.89 (1H, s, OH), 4.51 (1H, t, J: 6.5 Hz, CH), 5.95 (2H, s, OCH\(_2\)O), 6.78 (2H, br s, Ar), 6.87 (1H, s, Ar). \(\delta_C\): 10.5, 32.2, 76.3, 101.3, 106.8, 108.4, 119.8, 139.1, 147.2, 148.1.

**1-(3,4,5-Trimethoxyphenyl)propan-1-ol (11).**\(^{20}\) The same procedure described for the preparation of 3 was carried out with ethylmagnesium bromide (14 mmol in 7 mL of THF) and 3,4,5-trimethoxybenzaldehyde (6.53 mmol in 2 mL of THF) afforded 11 as clear oil (1.12 g , 39%).

NMR data: \(\delta_H\): 0.94 (3H, t, J: 6.0 Hz, CH\(_3\)), 1.77 (2H, m, CH\(_2\)), 2.09 (1H, s, OH), 3.83 (3H, s, OCH\(_3\)), 3.86 (6H, s, OCH\(_3\)), 4.52 (1H, t, J: 6.0 Hz, CH), 6.57 (2H, s, Ar). \(\delta_C\): 10.6, 32.3, 56.2 (2), 61.2, 76.6, 103.2 (2), 137.5, 140.9, 153.6 (2).

**1-(3,4-Dimethoxyphenyl)propan-1-ol (13).**\(^{21}\) The same procedure described for the preparation of 3 was carried out with ethylmagnesium bromide (28 mmol in 14 mL of THF) and 3,4-dimethoxybenzaldehyde (13.1 mmol in 2 mL of THF) afforded 13 as clear oil (2.0 g, 78%).

NMR data: \(\delta_H\): 0.88 (3H, t, J: 6.3 Hz, CH\(_3\)), 1.69 (1H, m, J: 6.3, 7.5 and 13.8 Hz, CH\(_2\)), 1.79 (1H, m, J: 6.3, 7.3 and 13.8 Hz, CH\(_2\)), 2.26 (1H, s, OH), 3.84 (3H, s, OCH\(_3\)), 3.86 (3H, s, OCH\(_3\)), 4.49 (1H, t, J: 6.6 Hz, CH), 6.81 (1H, d, J: 8.1 Hz, Ar), 6.83 (1H, dd, J: 1.6 and 8.1 Hz, Ar), 6.88 (1H, d, J: 1.5 Hz, Ar). \(\delta_C\): 10.6, 32.2, 56.2, 56.3, 76.2, 109.4, 113.3, 118.6, 137.7, 148.7, 149.3.

**r-1-Ethyl-c-2-methyl-t-3-(3,4-methylenedioxyphenyl)-5,6-methylenedioxyindane (7).** General procedure was carried out using alcohol 6 (0.100 g, 0.55 mmol), styrene 5 (0.0891 g, 0.55 mmol) and SnCl\(_4\) (0.185 g, 0.71 mmol) afforded a mixture of 7 and 80 (7:1) as an oil (140 g, 78%). The NMR spectra were coincident with those informed in lit.\(^{10}\)

**r-1-Ethyl-c-2-methyl-t-3-(3,4,5-trimethoxyphenyl)-4,5,6-trimethoxyindane (10).** General procedure was carried out using alcohol 11 (0.0246 g, 0.1086 mmol), styrene 9 (0.0891 g, 0.55 mmol) and SnCl\(_4\) (0.036 g, 0.14 mmol) afforded 10 as clear oil (0.0276 g, 61%). This compound was obtained by cycldimerization of styrene 9 (130 mg, 0.57 mmol) with MPA/S (58 mg) using the procedure indicated above. Yield 78 mg (66%).

NMR data: \(\delta_H\): 0.95 (3H, t, J: 7.4 Hz, CH\(_2\)CH\(_3\)), 1.01 (3H, d, J: 6.9 Hz, CHCH\(_3\)), 1.58 (2H, m, CH\(_2\)CH\(_3\)), 2.46 (1H, m, CHCH\(_3\)), 3.00 (1H, m, CHCH\(_2\)), 3.49 (3H, s, OCH\(_3\)), 3.76 (6H, s,
OCH₃), 3.80 (3H, s, OCH₃), 3.81 (3H, s, OCH₃), 3.87 (3H, s, OCH₃), 3.90 (1H, d, J: 5.1 Hz, CHPh), 6.28 (2H, s, Ar), 6.56 (1H, s, Ar). δC: 12.9, 15.4, 22.5, 48.3, 48.9, 56.6, 56.7, 56.8, 60.9, 61.5, 104.0, 105.3, 130.1, 136.8, 141.4, 143.6, 151.0, 153.5, 153.8. Calcd. for C₂₄H₃₂O₆ C 69.21, H 7.74; found C 69.02, H 7.80.

**r-1-Ethyl-c-2-methyl-t-3-(2,4,5-trimethoxyphenyl)-5,6-methylene dioxyindane (12).** General procedure was carried out using alcohol 6 (0.090 g, 0.5 mmol), styrene 1 (0.104 g, 0.5 mmol) and SnCl₄ (0.169 g, 0.65 mmol) afforded by p-tlc (hexane: ethyl acetate, 80:20) 12 as clear oil (0.0839 g, 46%).

NMR data: δH: 0.99 (3H, t, J: 7.3 Hz, CH₂CH₃), 1.03 (3H, d, J: 7.1 Hz, CHCH₃), 1.49 (1H, m, J: 7.3, 7.3 and 14.9 Hz, CH₂CH₃), 1.69 (1H, m, CH₂CH₃), 2.51 (1H, m, J: 6.8, 7.1 and 8.3 Hz, CHCH₃), 2.90 (1H, m, CHCH₂), 3.72 (3H, s, OCH₃), 3.85 (3H, s, OCH₃), 3.92 (3H, s, OCH₃), 4.31 (1H, d, J: 8.4 Hz, CHAr), 5.90 (1H, d, J: 1.5 Hz, O-CH₂-O), 5.92 (1H, d, J: 1.5 Hz, O-CH₂-O), 6.39 (1H, s, Ar), 6.46 (1H, s, Ar), 6.60 (1H, s, Ar), 6.75 (1H, s, Ar). δC: 12.8, 14.6, 22.6, 48.7, 48.8, 49.0, 56.7, 57.2, 57.4, 98.3, 101.3, 105.9, 106.2, 112.8, 124.4, 139.9, 141.2, 143.8, 146.5, 146.9, 148.4, 153.0. Calcd. for C₂₂H₂₂O₅ C 71.33, H 7.07; found C 71.12, H 7.10.

**r-1-Ethyl-c-2-methyl-t-3-(2,4,5-trimethoxyphenyl)-5,6-dimethoxyindane (14).** General procedure was carried out using alcohol 13 (0.090 g, 0.464 mmol), styrene 1 (0.104 g, 0.5 mmol) and SnCl₄ (0.156 g, 0.3 mmol) afforded 14 as an oil (0.149 g, 84%).

NMR data: δH: 0.96 (3H, t, J: 7.4 Hz, CH₂CH₃), 1.02 (3H, d, J: 7.2 Hz, CHCH₃), 1.55 (1H, m, J: 7.4, 7.7 and 13.6 Hz, CH₂CH₃), 1.75 (1H, m, J: 6.9, 7.4 and 13.6 Hz, CH₂CH₃), 2.43 (1H, m, J: 6.9, 7.2 and 7.9 Hz, CHCH₃), 2.91 (1H, m, CHCH₂), 3.65 (3H, s, OCH₃), 3.74 (3H, s, OCH₃), 3.84 (3H, s, OCH₃), 3.90 (3H, s, OCH₃), 3.91 (3H, s, OCH₃), 4.33 (1H, d, J: 7.9 Hz, CHAr), 6.38 (1H, s, Ar), 6.45 (1H, s, Ar), 6.59 (1H, s, Ar), 6.79 (1H, s, Ar). δC: 12.9, 14.7, 22.7, 48.9, 49.0, 49.5, 56.6, 56.7, 56.8, 57.2, 57.4, 98.4, 108.7, 108.8, 112.9, 124.9, 138.6, 140.2, 143.8, 148.2, 148.4, 148.6, 153.0. Calcd. for C₂₃H₂₃O₆ C 71.48, H 7.82; found C 71.35, H 7.85.

**r-1-Ethyl-c-2-methyl-t-3-(2,4,5-trimethoxyphenyl)-4,5,6-trimethoxyindane (15).** General procedure was carried out using alcohol 11 (0.104 g, 0.464 mmol), styrene 1 (0.112 g, 0.54 mmol) and SnCl₄ (0.156 g, 0.3 mmol) afforded 15 as an oil (0.187 g, 98%). NMR data: δH: 0.95 (3H, t, J: 7.4 Hz, CH₂CH₃), 0.97 (3H, d, J: 6.9 Hz, CH₂CH₃), 1.54 (1H, m, J: 6.1, 7.2 and 13.3 Hz, CH₂CH₃), 1.73 (1H, m, J: 6.1, 7.2 and 13.3 Hz, CH₂CH₃), 2.36 (1H, m, J: 3.6, 6.9 and 7.2 Hz, CHCH₃), 2.93 (1H, m, CHCH₂), 3.54 (3H, s, OCH₃), 3.58 (3H, s, OCH₃), 3.81 (3H, s, OCH₃), 3.87 (6H, s, OCH₃), 3.88 (3H, s, OCH₃), 4.33 (1H, d, J: 3.6 Hz, CHAr), 6.15 (1H, s, Ar), 6.56 (2H, s, Ar). δC: 12.9, 15.3, 22.0, 46.6, 48.2, 48.5, 56.6, 57.2, 57.2, 60.7, 61.4, 98.2, 103.5, 112.5, 125.3, 129.6, 141.0, 143.1, 143.8, 148.2, 150.9, 152.0, 153.5. Calcd. for C₂₄H₂₃O₆ C 69.21, H 7.74; found C 69.15, H 7.78.

**r-l-Ethyl-t-2-methyl-c-3-(4-methoxyphenyl)-4,5,7-trimethoxyindane (17).** General procedure was carried out using alcohol 3 (0.050 g, 0.22 mmol), styrene 16 (0.037 g, 0.25 mmol) and SnCl₄ (0.074 g, 0.28 mmol) afforded by p-tlc (CH₂Cl₂) 17 as white solid, mp: 82-84 °C (0.0315 g, 41%).

NMR data: δH: 0.91 (3H, t, J: 7.5 Hz, CH₂CH₃), 1.19 (3H, d, J: 6.9 Hz, CHCH₃), 1.63 (1H, m,
CH₂CH₃), 1.94 (1H, m, J: 3.3, 7.5 and 14.9 Hz, CH₂CH₃), 2.12 (1H, m, J: 5.3, 5.5 and 6.9 Hz, \( \text{CHCH}_3 \)), 2.75 (1H, m, J: 3.3, 5.5 and 8.6 Hz, \( \text{CHCH}_2 \)), 3.25 (3H, s, OCH₃), 3.80 (3H, s, OCH₃), 3.85 (3H, s, OCH₃), 3.86 (3H, s, OCH₃), 3.88 (1H, d, J: 5.3 Hz, CHAr), 6.44 (1H, s, Ar), 6.84 (2H, d, J: 8.8, Ar), 7.09 (2H, d, J: 8.8, Ar). δ₇C: 12.1, 22.0, 26.8, 49.6, 52.9, 55.8, 56.2, 57.1, 57.5, 60.4, 97.5, 114.1, 127.5, 129.3, 139.5, 140.3, 140.5, 152.8, 152.9, 158.3. Calcd. for C₂₂H₂₈O₄

\[ \text{r-1-Ethyl-3-methyl-2-(4-methoxyphenyl)-6,4,5,6-trimethoxindane (18). General procedure was carried out using alcohol \( \text{CHCl}_2 \) (0.113 g, 0.5 mmol), styrene (0.074 g, 0.5 mmol) and SnCl₄ (0.166 g, 0.64 mmol). Afforded by p-tlc (CH₂Cl₂) 18 as clear oil (0.0935 g, 53%). NMR data: δ₁H: 0.98 (3H, t, J: 7.4 Hz, CH₂CH₃), 1.02 (3H, d, J: 7.1 Hz, CHCH₃), 1.62 (2H, m, CH₂CH₃), 2.47 (1H, m, J: 5.3, 7.1 and 7.1 Hz, CHCH₃), 3.04 (1H, m, CH₂CH₃), 3.47 (3H, s, OCH₃), 3.80 (3H, s, OCH₃), 3.82 (3H, s, OCH₃), 3.90 (3H, s, OCH₃), 3.95 (1H, d, J: 5.1 Hz, CHAr), 6.59 (1H, s, Ar), 6.82 (2H, d, J: 8.8 Hz, Ar). δ₇C: 12.9, 15.2, 22.5, 48.4, 48.7, 55.4, 55.7, 56.7, 60.7, 61.4, 103.9, 114.0, 129.0, 130.5, 137.5, 141.3, 143.4, 150.9, 153.6, 158.4. Calcd. for C₂₂H₂₈O₄

\[ \text{r-1-Ethyl-3-methyl-2-(4-methoxyphenyl)-5,6-dimethoxindane (19). General procedure was carried out using alcohol \( \text{CHCl}_2 \) (0.098 g, 0.5 mmol), styrene (0.074 g, 0.5 mmol) and SnCl₄ (0.166 g, 0.64 mmol). Afforded by p-tlc (CH₂Cl₂) 19 as clear oil (0.090 g, 55%). NMR data: δ₁H: 1.00 (3H, t, J: 7.3 Hz, CH₂CH₃), 1.06 (3H, d, J: 7.1 Hz, CHCH₃), 1.42 (1H, m, J: 7.3, 8.9 and 14.7 Hz, CH₂CH₃), 1.73 (1H, m, J: 5.9, 7.3 and 14.9 Hz, CH₂CH₃), 2.47 (1H, m, J: 7.1, 7.1 and 9.1 Hz, CHCH₃), 2.95 (1H, m, J: 5.9, 7.1 and 8.9 Hz, CHCH₂), 3.75 (3H, s, OCH₃), 3.84 (4H, OCH₃ and CHAr), 3.92 (3H, s, OCH₃), 6.44 (1H, s, Ar), 6.83 (1H, s, Ar), 6.88 (2H, d, J: 8.6 Hz, Ar), 7.09 (2H, d, J: 8.9 Hz, Ar). δ₇C (CDCl₃): 12.9, 14.3, 23.0, 49.1, 50.3, 55.8, 56.6, 56.7, 57.1, 108.6, 108.7, 114.3, 130.0, 136.8, 138.8, 140.0, 148.2, 148.7, 158.7. Calcd. for C₂₁H₂₆O₃

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References


