Research article

MRC

Received: 14 November 2016 Revised: 2 December 2016 Accepted: 6 December 2016 Published online in Wiley Online Library

(wileyonlinelibrary.com) DOI 10.1002/mrc.4564

Effect of methoxyl groups on the NMR spectra: configuration and conformation of natural and synthetic indanic and tetralinic structures

Beatriz Lantaño,[a,b]* José M. Aguirre,[a] Eleonora V. Drago,[a] Diego J. de la Faba,[a] Nicolás Pomilio[b] and Jorge D. Mufato[a]**

Here, we studied the influence of the methoxyl groups attached at C-7 and C-2′ of natural and synthetic 1-arylindanes on the chemical shift of the signal of bibenzylic hydrogen and carbon atoms and $J_{1,2}$ coupling constants. This influence was also analysed in natural 1-aryltetralins and related compounds that possess methoxyl and/or hydroxyl groups bound at C-8 and C-2′. The methoxyl groups attached at C-7 in indanes or at C-8 in tetralins produce a deshielding signal at H-1 and shield at C-1 and a strong decrease in the value of $J_{1,2}$ due to the *pseudoequatorial* location adopted by the aryl group bound at C-1, avoiding an '$A^{1,3}$ *strain*'. Furthermore, compounds with hydroxyl or methoxyl groups in C-2′, in the absence of substituents of C-7 or C-8, present a strong deshielding signal at H-1, strong shield of the C-1 signal and a decrease in the value of $J_{1,2}$. This is attributed to the stereoelectronic effects of the methoxyl or hydroxyl groups, which we have called '*Asarone effect*'. NOESY experiments were conducted to confirm the configuration and conformation of some of the compounds included in this work. This study shows that both effects, $A^{1,3}$ *strain* and *Asarone effect*, must be taken into account when the structure of natural indanes and tetralins is analysed by using ^{1}H-NMR and ^{13}C-NMR spectra. Copyright © 2016 John Wiley & Sons, Ltd.

Keywords: indans; tetralins; ^{1}H-NMR; ^{13}C-NMR

Introduction

Cyclodimers with indanic structure derived from natural (*E*)-*β*-methylstyrenes (Isohomogenol and Isosafrole) and synthetic (*E*)-*β*-methylstyrenes have been described earlier (Scheme 1).[1]

The configurational assignment of the four possible diastereomers led to several controversies until 1969, when MacMillan *et al.*[2] established the relative configuration of isomers *α*, *β* and *γ* of Isohomogenol and Isosafrole by using ^{1}H-NMR (Fig. 1).

This contribution has been of significant importance and is widely mentioned in the literature for the configurational assignment of these kinds of structures.[3]

However, based on works mentioned in the preceding texts, some authors[4] have incorrectly assigned the configuration to cyclodimers derived from (*E*)-*β*-methylstyrenes.

The *γ* configuration of the only indanic cyclodimer isolated from the natural styrene Asarone (Scheme 1) has been assigned by X-ray diffraction.[5] This compound shows low values of $J_{1,2}$ and $J_{2,3}$ (~4 Hz), which are not consistent with data published by MacMillan[2] for any of the diastereomers studied. Alesso *et al.*[6] reported that in cyclodimerization processes of (*E*)-*β*-methylstyrenes, the presence of methoxyl groups at C-2 and C-5 of the aryl group is determinant for the stereoselectivity of the reaction. The *γ*-diasarone has methoxyl groups at C-4, C-7 and C-2′, which influence the coupling constants of benzylic hydrogens and the chemical shift of hydrogen and carbon atoms. On the other hand, several stereodirected syntheses of diastereomers of 1,2,3-trisubstituted indanic structures have been developed, and the configurational assignments have been supported by 1D and 2D NMR studies.[7] Other indanic and tetralinic structures obtained by cyclodimerization of natural stilbenes, as resveratrol and ixyresveratrol, and synthetic stilbenes present remarkable differences in the ^{1}H-NMR and ^{13}C-NMR spectra, with similar structures that do not have methoxyl groups at C-7 or C-8 of the indanic and the tetralinic rings respectively.[8] These differences are also observed in tetralinic bisnorlignans derived from 2,4,5-trimethoxystyrene such as pachypostaudins A and B (Scheme 2).[9]

Herein, we studied the influence of the methoxyl groups attached at C-7 and C-2′ of indanes on the chemical shift of bibenzylic hydrogen and carbon atoms and coupling constants $J_{1,2}$. This analysis was extended to tetralinic structures with methoxyl groups at C-8 and C-2′. Model indanic and tetralinic structures with a different substitution pattern at sp^3 carbons and aromatic rings were synthesized. We also aimed to shed light on the scopes and limitations of NMR as a tool for the configurational assignment of natural and synthetic indanic and tetralinic cyclodimers formed from styrene, (*E*)-*β*-methylstyrenes and stilbenes.

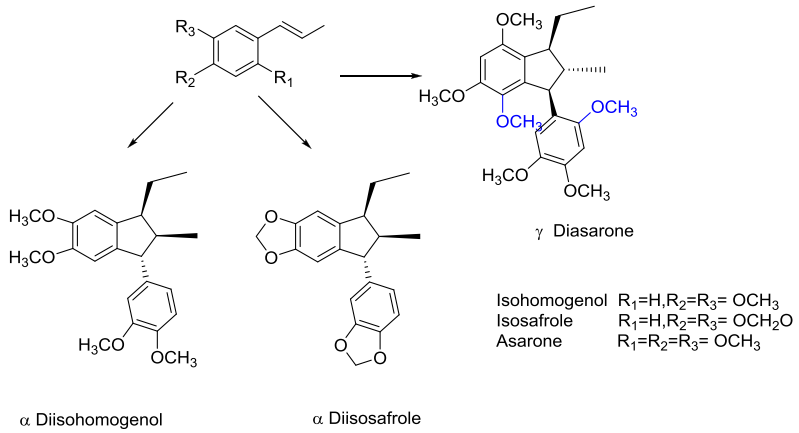
* *Correspondence to: Beatriz Lantaño, Cátedra de Química Orgánica II, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, 1113 Ciudad de Buenos Aires, Argentina. E-mail: lantanob@gmail.com*

** *Correspondence to: José M. Aguirre, Departamento de Ciencias Básicas, Universidad Nacional de Luján, Ruta 5 y Av. Constituci, 6700, Argentina. E-mail: jaguirre@hotmail.com*

a *Departamento de Ciencias Básicas, Universidad Nacional de Luján, Ruta 5 y Av. Constituci, 6700, Argentina*

b *Cátedra de Química Orgánica II, Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 956, 1113, Ciudad de Buenos Aires, Argentina*

Copyright © 2016 John Wiley & Sons, Ltd.



Scheme 1. Indanic cyclodimers from natural (*E*)-β-methylstyrenes.

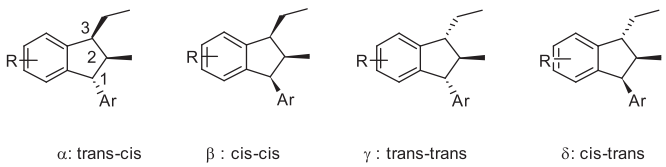
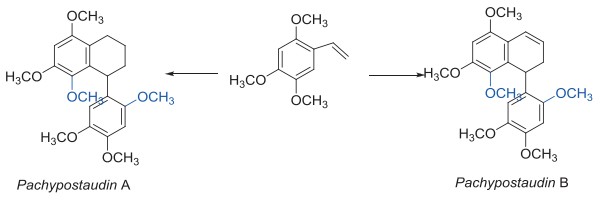


Figure 1. Diastereomers of 3-ethyl-2-methyl-1-aryilindanes.



Scheme 2. Tetralinic cyclodimers from a natural styrene.

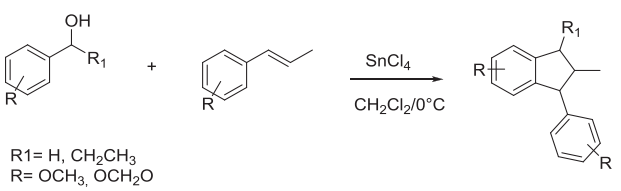
Results and Discussion

Synthesis of substituted indanes and tetralins

Synthesis of 1-arylindanes

Compounds **1**–**17** were obtained by the formal cycloaddition reaction [3 + 2] (*CAF [3 + 2]*) from benzylic alcohols, β-methylestyrenes and $SnCl_4$ as catalyst[10] (Scheme 3 and Table 1).

The structure and configuration of model-synthesized indanes (**1**–**4**) were established by 1D and 2D NMR, and they all have *trans* configuration. The indanes 1,2,3-trisubstituted in the pentagonal ring were obtained as α and/or γ diastereomers, and in those having substituents at C-4 and C-7, the predominant diastereomer is γ.



Scheme 3. Synthesis of 1-arylindanes **1**–**17**.

Synthesis of 1-aryltetralins

Tetralins **24** and **26**–**28** were obtained from the suitable substituted 1-tetralone and the arylmagnesium reagent followed by hydrogenolysis[7,11] (Scheme 4 and Table 2). The structure was confirmed by NMR spectroscopy.

Synthesis of 1,2,3-triaryltetralins

Tetralins **30**–**32** and **36** were synthesized by dimerization catalysed by Lewis acids, using the respective *trans*-stilbenes as starting material (Scheme 5 and Table 3). The structure and the stereochemistry of **31** and **32** have been previously published by us.[8] The ^{1}H-NMR data for **30** and **36** have been published by Hiscock and Porter,[13] although the authors only assigned the configuration of isomer **31**. Based on HSQC, HMBC and NOESY experiments, we established that the configuration for **36** is *1,2-trans-2,3-cis* (Table 4).

NMR spectroscopy of substituted indanes and tetralins

NMR spectral analysis of 1,2-substituted indanes

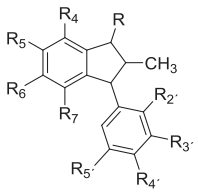
The configuration of the model indanes **1**–**4** was supported by NMR data. The *trans* arrangement was assigned, considering the chemical shifts for the hydrogens and the carbon of the methyl group attached at C-2, δ_H 1.14–1.17 p.p.m. and δ_C 17.1–20.0 p.p.m. (Fig. 2 and Table 5).

The values of these chemical shifts correspond to methyl groups which, in this kind of structure, do not significantly experience the influence of a substituent on a neighbour carbon atom (low-shielding *γ-gauche* effect).[14] The value of the $J_{1,2}$ coupling constants (9.5 and 8.5 Hz respectively) in compounds **1** and **2** are indicative of H-1-*pseudoaxial*/H-2-*axial* arrangement.

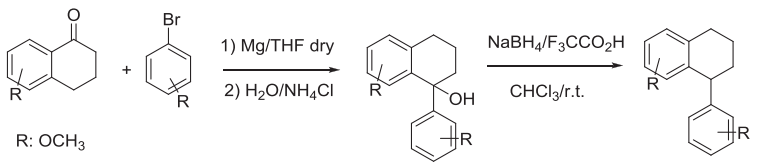
The ^{1}H-NMR spectra of cycloadduct **2** show a deshielding of the signal at H-1 (δ: 4.28 p.p.m.) relative to compound **1** (δ: 3.70 p.p.m.) and a lower value of $J_{1,2}$ (ΔJ = 1 Hz). This effect is due to the influence of the methoxyl group attached at C-2′ of the unfused aryl group, which produces a stereoelectronic effect on H-1. On the other hand, the chemical shifts of C-1 and C-2 in cycloadduct **2** show a strong shielding effect [$\Delta\delta_C$: 6.2 (C-1) and 4.0 (C-2)] relative to cycloadduct **1** due to the shielding *γ-gauche* effect.[7] This shielding effect indicates that the aryl group attached at C-1 has a spatial position in which the oxygen of the methoxyl group attached at C-2′ is coplanar to C-1 and that the C-2′ of the aryl

Copyright © 2016 John Wiley & Sons, Ltd.

Table 1. Synthesized substituted 1-arylindanes

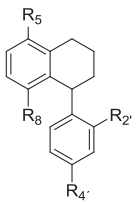


Compound	$R_{2'}$	$R_{3'}$	$R_{4'}$	$R_{5'}$	R_4	R_5	R_6	R_7	R	Configuration C-1–C-2/C-2–C-3	Diast
1	H	H	OCH_3	H	H	OCH_3	OCH_3	H	H	*trans*	*trans*
2[10]	OCH_3	H	OCH_3	OCH_3	H	OCH_3	OCH_3	H	H	*trans*	*trans*
3	H	H	OCH_3	H	H	OCH_3	OCH_3	OCH_3	H	*trans*	*trans*
4	OCH_3	H	OCH_3	OCH_3	H	OCH_3	OCH_3	OCH_3	H	*trans*	*trans*
5[2,6,10]	H	OCH_2O		H	H	OCH_2O		H	CH_2CH_3	*trans-cis*	α
6	OCH_3	H	H	H	H	OCH_3	OCH_3	H	CH_2CH_3	*trans-cis*	α
7[10]	OCH_3	H	OCH_3	OCH_3	H	OCH_3	OCH_3	H	CH_2CH_3	*trans-cis*	α
8[6]	OCH_3	H	OCH_3	OCH_3	H	OCH_2O		H	CH_2CH_3	*trans-cis*	α
9[6]	H	H	OCH_3	H	H	OCH_3	OCH_3	OCH_3	CH_2CH_3	*trans-cis*	α
10[6]	H	OCH_3	OCH_3	OCH_3	H	OCH_3	OCH_3	OCH_3	CH_2CH_3	*trans-cis*	α
11	OCH_3	H	H	H	H	OCH_3	OCH_3	OCH_3	CH_2CH_3	*trans-cis*	α
12[10]	OCH_3	H	OCH_3	OCH_3	H	OCH_3	OCH_3	OCH_3	CH_2CH_3	*trans-cis*	α
13[6]	H	OCH_2O		H	H	OCH_2O		H	CH_2CH_3	*trans-trans*	γ
14[6,10,7]	OCH_3	H	OCH_3	OCH_3	OCH_3	H	OCH_3	OCH_3	CH_2CH_3	*trans-trans*	γ
15[10]	H	H	OCH_3	H	OCH_3	H	OCH_3	OCH_3	CH_2CH_3	*trans-trans*	γ
16[10]	OCH_3	H	OCH_3	OCH_3	H	OCH_3	OCH_3	H	CH_2CH_3	*trans-trans*	γ
17	OCH_3	H	OCH_3	OCH_3	H	OCH_2O		H	CH_2CH_3	*trans-trans*	γ

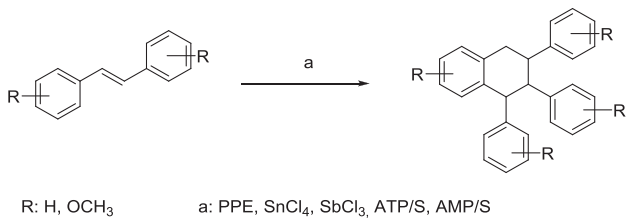


Scheme 4. Synthesis of 1-aryltetralins **24**–**28**.

Table 2. Synthesized substituted 1-arylitetralins



Compound	R_5	R_8	$R_{2'}$	$R_{4'}$
24[12]	H	H	H	OCH_3
26	H	H	OCH_3	OCH_3
27	OCH_3	OCH_3	H	H
28	OCH_3	OCH_3	OCH_3	OCH_3



Scheme 5. Synthesis of 1,2,3-triaryltetralins **30**–**36**.

group and the C-2 of the pentagonal ring are in a gauche arrangement (Table 5).

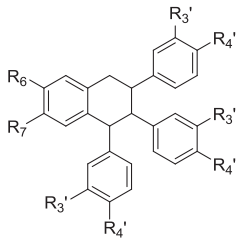
In this study, the striking unshielding effect of the bibenzylic hydrogen atoms (H-1), the decrease in the coupling constant ($J_{1,2}$) and the shielded bibenzylic carbon atoms (C-1) observed in 1-aryl substituted indanic structures have been collectively named '*Asarone effect*'.[15]

Another observation to highlight is that indane **3** shows $J_{1,2}$ 4.7 Hz, which is significantly lower than that observed in compound **1** and than that expected in a *trans* arrangement (H-H-1-*pseudoaxial*/H-2-*axial*). This difference is due to the fact that in indane **3**, the conformation of the pentagonal ring locates the aryl group attached at C-1 in the *pseudoaxial* position because of the presence of the methoxyl group at C-7 (Fig. 3).

In this conformation, the '$A^{1,3}$ *strain*' is avoided.[16] This assertion was confirmed by a NOESY experiment.

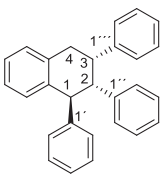
Copyright © 2016 John Wiley & Sons, Ltd.

Table 3. Synthesized substituted 1,2,3-aryltetralins



Compound	R_6	R_7	$R_{3'}$	$R_{4'}$	Configuration C-1–C-2/C-2–C-3	Diastereomer
36[13]	H	H	H	H	*trans-cis*	α
30[13]	H	H	H	H	*trans-trans*	γ
31[8]	OCH_3	OCH_3	OCH_3	OCH_3	*trans-trans*	γ
32[8]	H	OCH_3	H	OCH_3	*trans-trans*	γ

Table 4. NMR spectral data of compound **36** ($CDCl_3$, 500 MHz)



Position	^1H	^{13}C	HMBC	NOESY
1	4.57 [1H, doublet (d), 2.6]	50.11	C-8, C-8a, C-1′, C-1″	H-2′, H-2″
2	3.40 [1H, triplet (t), 3.1, 3.3]	54.59	C-8a	H-2′, H-2″, H-2‴
3	3.57 (1H, ddd, 9.7, 6.3, 3.5)	39.37	C-1″, C-1‴, C-2′	H-2′, H-2″
4	3.08 [2H, multiplet (m)]	30.60	C-4a, C-5	H-2′, H-2″, H-2‴
4a	—	137.56	—	—
5	7.05 (1H,m)	126.08	—	—
8	6.99 (1H, m)	130.85	—	—
8a	—	137.83	—	—
1′	—	147.76	—	—
2′	7.10 (2H, m)	128.29	—	H-1, H-4
1″	—	141.32	—	—
2″	6.58 (2H, d, 7.0)	128.20	—	H-1, H-2, H-4
1‴	—	142.97	—	—
2‴	6.69 [2H, doublet doublet (dd), 2.0, 5.5]	127.74	—	H-3, H-4

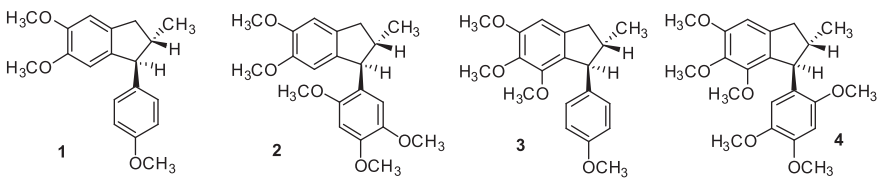


Figure 2. Synthetic *trans*-1-Aryl-2-methylindanes.

Table 5. ^1H-NMR and ^{13}C-NMR spectral data of hydrogen and aliphatic carbon atoms of 1-arylindanes

Compound	$\delta_H CH_3$	$\delta_C CH_3$	δH-1	$J_{1,2}$	δC-1	δC-2	δC-3
1	1.16	18.17	3.70	9.5	58.79	46.77	40.08
2[10b]	1.15	17.91	**4.28**	8.5	**52.56**	**42.81**	39.58
3	1.17	19.99	3.88	**4.7**	56.11	45.27	40.48
4	1.14	17.10	**4.35**	**5.1**	**53.61**	**42.33**	40.84

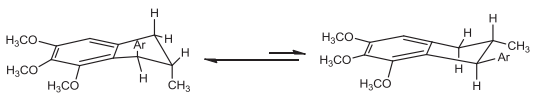


Figure 3. Conformational equilibrium of indane **3**.

The analysis of the data provided by NOESY experiment of **3** (Fig. 4 and Table 6) indicates that H-1 (δ 3.88 p.p.m.) correlates with hydrogens at δ1.17 p.p.m. from the methyl group attached at C-2

Copyright © 2016 John Wiley & Sons, Ltd.

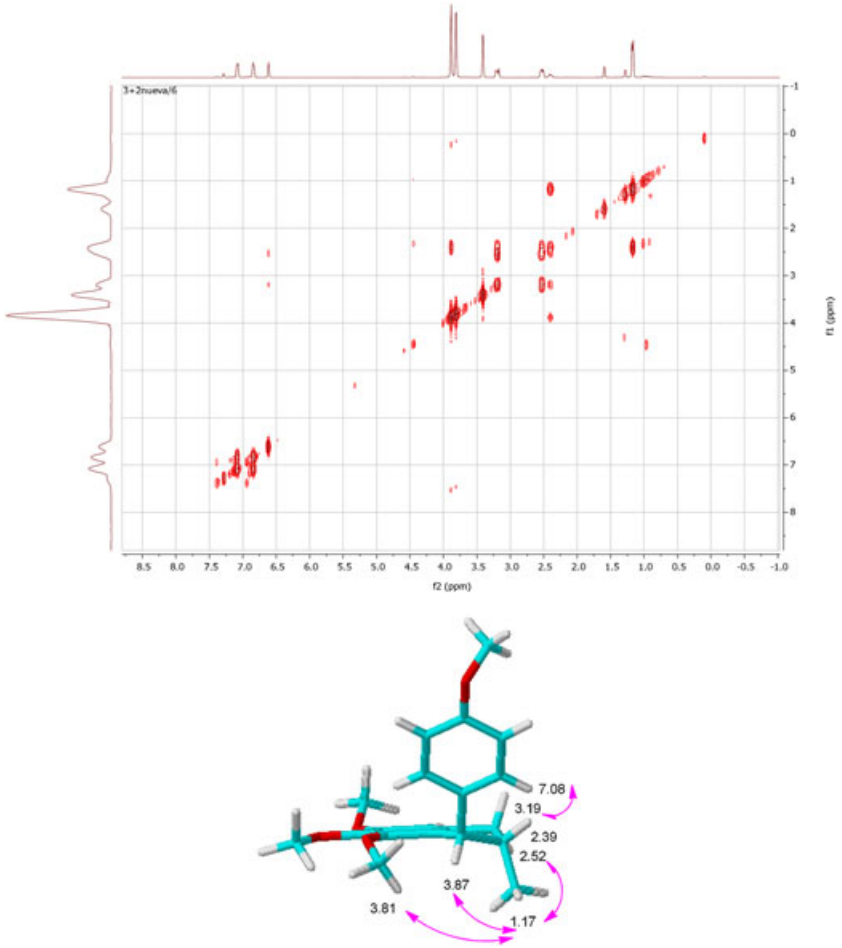


Figure 4. NOESY data of compound **3**.

Table 6. NMR spectral data of compound **3** ($CDCl_3$, 600 MHz)

Position	^1H	^{13}C	TOCSY	NOESY
1	3.8 7 (1H, d, 4.7)	56.98	—	H-2′, H-3α, CH_3
2	2.39 (1H, m)	45.27	—	—
3α	3.19 (1H, dd, 7.7, 15.6)	40.48	C-3a, C-7a	H-2′, H-4
3β	2.52 (1H, dd, 6.7, 15.6)	40.48	C-3a	—
3a	—	139.08	—	—
4	6.61 [1H, singlet (s)]	103.44	C-3, C-5, C-6	OCH_3(C-5)
5	—	153.29	—	—
6	—	140.83	—	—
7	—	150.38	—	—
CH_3	1.17 (3H, d, 6.8)	19.99	—	—
OCH_3(C-5)	3.88 (3H, s)	56.11	C-5	—
OCH_3(C-6)	3.40 (3H, s)	60.05	—	H-4
OCH_3(C-7)	3.81 (3H, s)	60.87	—	H-2′
1′	—	137.82	—	—
2′	7.08 (2H, d, 8.6)	128.43	C-3, C-4′	OCH_3(C-7)
3′	6.84 (2H, d, 8.6)	113.56	C-3′, C-4′	—
4′	—	157.86	—	—
OCH_3(C-4′)	3.81 (3H, s)	55.21	C-3a	—

because H-1 and CH_3(C-2) are in a *cis* arrangement. Furthermore, the hydrogens of CH_3(C-2) correlate with the hydrogens of the methoxyl group attached at C-7 (δ 3.81 p.p.m.).

The correlations described are only possible in the conformation where the aryl group attached at C-1 is in a *pseudoaxial* position and the methyl group is *axial*.

Copyright © 2016 John Wiley & Sons, Ltd.

Table 7. ^{1}H-NMR spectral data of the aliphatic hydrogen atoms of 1-aryl-3-ethyl-2-methylindanes

Compound	H-1	H-2	H-3	CH_3	CH_2CH_3	CH_2CH_3	$J_{1,2}$	$J_{2,3}$
α-Diisohomogenol[2]	3.77	2.4	2.90	1.04	1.65	0.96	9.5	7.25
β-Diisohomogenol[2]	4.27	2.77	2.95	0.47	1.61	1.07	7.0	7.0
γ-Diisohomogenol[2]	3.65	2.00	2.69	1.15	1.80	1.00	9.0	9.0
?-Diisoeugenol[4]	3.73	2.4–2.5	2.86–2.95	1.03	1.31–1.441.65–1.75	0.97	9.4	No data
?-Diisoeugenol[4]	3.73	2.4–2.5	2.85–2.95	1.03	1.31–1.441.65–1.75	0.97	9.5	No data

Nuclear magnetic resonance spectroscopic data indicate that indane **4** adopts the conformation which avoids the $A^{1,3}$ *strain* ($J_{1,2}$ 5.1 Hz) and presents the *Asarone effect* ($\delta_{H\text{-}1}$ 4.35 p.p.m.; $J_{1,2}$ 5.1 Hz, $\delta_{C\text{-}1}$: 53.6 p.p.m. and $\delta_{C\text{-}2}$ 42.3 p.p.m.; Table 5).

NMR spectral analysis of 1,2,3-trisubstituted indanes

Because this kind of compound can appear as four racemic diastereomers named ***α***, ***β***, ***γ*** and ***δ*** (Fig. 1), the configuration of cyclodimers ***α***, ***β*** and ***γ*** was assigned by using the ^{1}H-NMR data reported by MacMillan *et al.*[2] The studies performed to dimerize Isohomogenol and Isosafrole show that the main isomers are ***α*** and ***γ***.[2,3] Nevertheless, Angle *et al.*[3] reported that in *CAF[3 + 2]*, the main diastereomers are ***α*** and ***β***. Through different synthetic pathways and cyclodimerization reactions, we obtained the diastereomers ***α***, ***β*** and ***γ***.[7,10] Tables 7 and 8 summarize the NMR data of aliphatic hydrogens and carbons (δ_H, δ_C and J_{HH}) of the indanes described in the literature and which have been broadly used for the configurational assignment of 1-aryl-3-ethyl-2-methylindanes, cyclodimers of β-methylestirenes.

The coupling constants $J_{1,2}$ and $J_{2,3}$ allow differentiating diastereomers ***β*** and ***γ*** from the other two because H-1 and H-3 show the same configurational relationship related to H-2 (Fig. 5).

Table 8. ^{13}C-NMR spectral data of the aliphatic carbon atoms of 1-aryl-3-ethyl-2-methylindanes

Compound	C-1	C-2	C-3	CH_3	CH_2CH_3	CH_2CH_3
α-Diisohomogenol[3]	56.7	49.3	48.3	13.6	22.2	12.0
β-Diisohomogenol[7d]	54.3	49.1	43.2	9.8	21.3	12.3
γ-Diisosafrole[3]	58.5	51.4	50.9	17.4	24.6	10.6
?-Diisoeugenol[4]	56.7	49.2	48.5	13.8	22.4	12.2
?-Diisoeugenol[4]	56.7	49.2	48.5	13.8	22.4	12.2

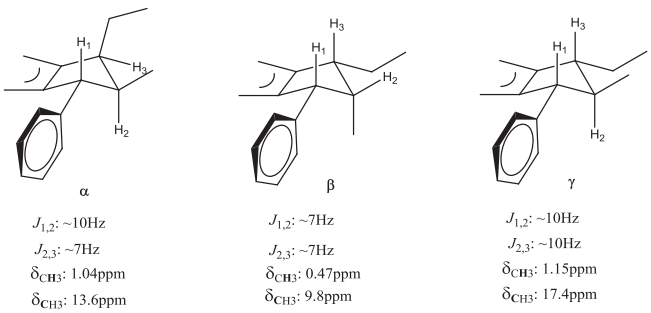


Figure 5. NMR data of diastereomers of 3-ethyl-2-methyl-1-aryilindanes.

Table 9. ^{1}H-NMR spectral data of the aliphatic hydrogen atoms of 1-aryl-3-ethyl-2-methylindanes: diastereomer ***α***

Compound	H-1	H-2	H-3	CH_3C-2	$J_{1,2}$	$J_{2,3}$
α-Diisohomogenol	**3.77**	2.11	2.90	1.04	**9.5**	**7.2**
β-Diisohomogenol	4.27	2.77	2.95	0.47	7.0	7.0
γ-Diisosafrole	3.57	1.99	2.65	1.14	9.3	9.3
5	3.70	2.46	2.90	1.00	9.4	7.3
6	**4.33**	2.44	2.90	0.99	**6.7**	6.9
7	**4.33**	2.43	2.91	1.02	**7.9**	7.2
8	**4.31**	2.51	2.90	1.03	**8.4**	6.8
9	3.95	2.47	3.04	1.02	**5.1**	7.1
10	3.90	2.46	3.00	1.01	**5.1**	7.2
11	**4.36**	2.35	2.91	0.96	**2.5**	6.9
12	**4.33**	2.36	2.93	0.97	**3.6**	7.2

Table 10. ^{13}C-NMR spectral data of the aliphatic carbon atoms of 1-aryl-3-ethyl-2-methylindanes: diastereomer ***α***

Compound	C-1	C-2	C-3	CH_3
α-Diisohomogenol	**56.7**	49.3	48.3	13.6
β-Diisohomogenol	54.3	49.1	43.2	9.8
γ-Diisosafrole	58.5	51.4	50.8	17.4
5	56.68	49.41	48.31	13.65
6	**50.33**	48.23	48.63	15.09
7	**49.49**	49.03	48.91	14.74
8	**49.05**	48.77	48.70	14.66
9	55.40	48.37	48.75	15.20
10	56.60	48.95	48.36	15.40
11	**46.14**	48.07	49.12	15.66
12	**46.57**	48.23	48.48	15.32

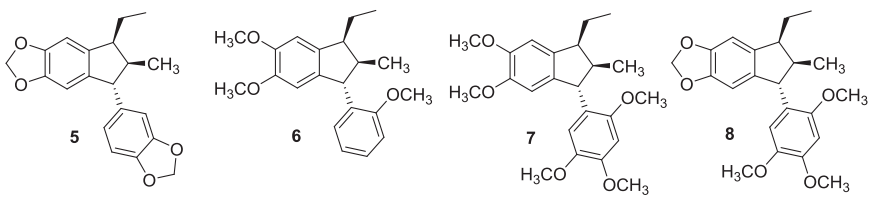


Figure 6. Synthetic 1,2-*trans*-2,3-*cis*-3-ethyl-2methyl-1-arylindanes (***α***).

Copyright © 2016 John Wiley & Sons, Ltd.

Instead, in isomer α, the spatial position of H-1/H-2 is *trans* and H-2/H-3 is *cis*, and thus the different values for $J_{1,2}$ and $J_{2,3}$ are ~10 and ~7 Hz respectively. Other relevant data are the chemical shifts of the hydrogen and carbon of the methyl group attached at C-2, which show different shielding effect due to the spatial relationship of the groups at C-1 and at C-3 in each isomer (Fig. 4).

Recently, Kouznetsov and Merchan Arenas[4] have reported a new and efficient stereoselective synthesis of γ-diisoeugenol and its large-scale preparation under green conditions, and Gonzalez de Castro and Jianliang[4] obtained the same cyclodimer to which configuration γ was assigned by catalysed selective oxidation of olefins to carbonyls with O_2. The evaluation of NMR data published

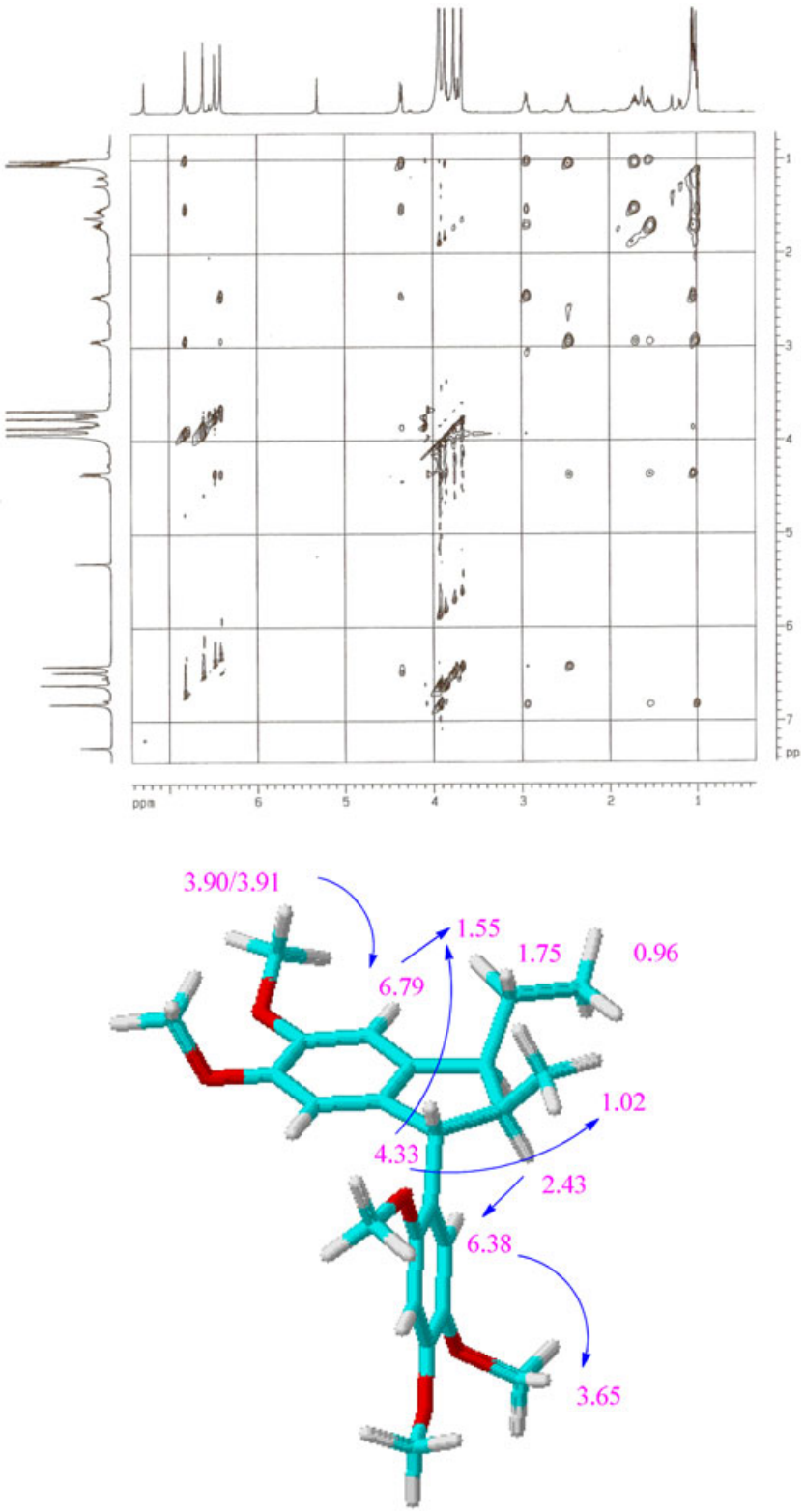


Figure 7. NOESY data of compound **7**.

Copyright © 2016 John Wiley & Sons, Ltd.

in both cases (Tables 7 and 8) indicates that the configurational assignment of the synthesized cyclodimers is not correct and corresponds to diastereomer ***α***.

3-Ethyl-2-methyl-1-arylindanes: diastereomer α. The ^{1}H-NMR and ^{13}C-NMR spectroscopic data of cycloadducts **5**–**12** (Fig. 6) are shown in Tables 9 and 10.

The configurational assignment of 1,2-*trans*-2,3-*cis*, diastereomer ***α***, was performed, considering the descriptions mentioned in the preceding texts, especially δ_H and δ_C of the methyl group attached at C-2. Nevertheless, it is necessary to study the differences observed from the spectroscopic data with the data previously published. The coupling constants $J_{2,3}$ of compounds **6**, **7** and **8** (7.2, 6.9 and 6.8 Hz respectively) are similar to those of indane **5**, which indicate a H-2/H-3 *cis* arrangement but differ in the chemical shift of H-1, unshielded in ~0.6 p.p.m., and in the value of $J_{1,2}$ (7.9, 6.7 and 8.4 Hz), which is lower than that found in **5** (~9.5 Hz). The three indanes also show that C-1 is remarkably shielded (~7 p.p.m.; Table 10). These differences are similar to those described for compound **2** and are related to the *Asarone effect*. In addition, a NOESY experiment of **7** was performed (Fig. 7 and Table 11) and showed that the H-1 at δ 4.33 p.p.m. correlates to the hydrogen at δ 1.55 p.p.m., which belongs to the methylene group of the ethyl moiety attached at C-3. This indicates that the H-1 and the methyl and the ethyl groups are in a *cis* arrangement. On the other hand, the correlation between H-2 (2.43 p.p.m.) and the aromatic hydrogen atoms (6.38 p.p.m.) determines that the aromatic ring attached at C-1 is *cis* related to H-2. These results are consistent to the ***α*** configuration assigned to compound **7** and also to **6** and **8**, by comparison.

Indanes **9**–**12** (Fig. 8) are all diastereomers ***α*** and show the same substitution pattern in the aromatic ring. The NMR analysis of **9** and **10** shows $J_{1,2}$ values (5.1 Hz) lower than those expected for a *trans diaxial* arrangement (Fig. 5). This difference is because both present a conformation in which the unfused ring is in a *pseudoaxial* position, avoiding the $A^{1,3}$ *strain*[16] as observed in compound **4**. The spatial relationship of H-2/H-3 is *gauche* in any of the possible extreme conformations. For this reason, the $J_{2,3}$ values do not show a significant variation. Moreover, compounds **11** and **12** have an aryl group at C-1 with a methoxyl group attached at C-2′ and show chemical shift of C-1, H-1 and $J_{1,2}$ consistent with the *Asarone effect* (Tables 9 and 10).

3-Ethyl-2-methyl-1-arylindanes: diastereomer γ

Indanes **13** (diisosafrole), **14** (diasarone) and **15**–**17** are diastereomers ***γ*** (Fig. 9). In all of them, the methyl group attached at C-2

Table 11. NMR spectral data of compound **7** ($CDCl_3$, 400 MHz)

Position	^{1}H	^{13}C	NOESY
1	4.33 (1H, d, 7.9)	49.49	H-α, H-4, CH_3(C-2)
2	2.43 (1H, m, 7.2, 7.9, 6.9)	49.03	H-3, H-6′, CH_3(C-2)
3	2.91(1H, m)	48.91	H-α, H-β, H-4, CH_2**CH_3**
3a	—	140.21	H-α, H-2, CH_2**CH_3**
4	6.79 (1H, s)	108.66	H-α, H-2, CH_2**CH_3**, OCH_3(C-5)
5	—	143.82	—
6	—	148.18	—
7	6.45 (1H, s)	108.77	OCH_3(C-6)
7a	—	138.57	—
CH-Hα	1.55 (1H, m, 7.4, 7.7, 13.6)	22.76	—
CH-Hβ	1.75 (1H, m, 6.9, 7.4, 13.6)	22.76	—
CH_2**CH_3**	0.96 (3H, t, 7.4)	12.95	—
CH_3(C-2)	1.02 (3H, d, 7.2)	14.74	—
OCH_3(C-5)	3.90 (3H, s)	57.46	—
OCH_3(C-6)	3.74 (3H, s)	56.61	—
1′	—	124.94	—
2′	—	152.98	—
3′	6.59 (1H, s)	98.39	OCH_3(C-4′)
4′	—	148.41	—
5′	—	148.66	—
6′	6.36 (1H, s)	112.94	OCH_3(C-5′)
OCH_3(C-2′)	3.91 (3H, s)	56.67	—
OCH_3(C-4′)	3.84 (3H, s)	56.75	—
OCH_3(C-5′)	3.65 (3H, s)	57.19	—

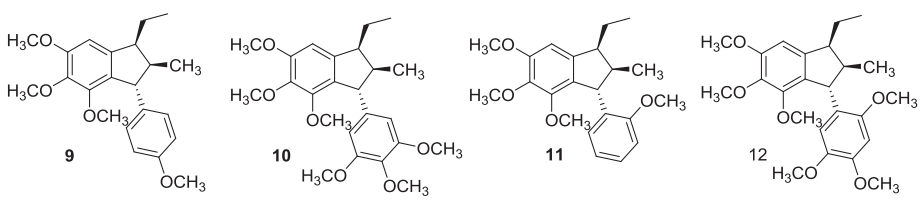


Figure 8. Synthetic 1,2-*trans*-2,3-*cis*-3-ethyl-2-methyl-1-aryl-7-methoxyindanes (***α***).

Copyright © 2016 John Wiley & Sons, Ltd.

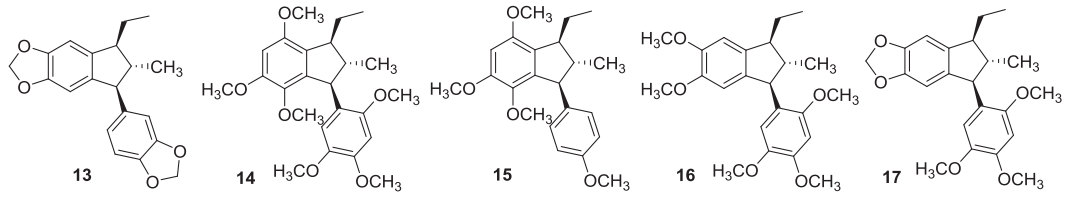


Figure 9. Synthetic 1,2-*trans*-2,3-*trans*-3-ethyl-2-methyl-1-arylindanes (*γ*).

shows close values of chemical shift of hydrogen and carbon atoms (Tables 12 and 13).

These data indicate a 1,2-*trans*-2,3-*trans* arrangement. Compounds **14** and **15** have the same substitution pattern at the aromatic ring of the indanic frame and show low and similar values of $J_{1,2}$ and $J_{2,3}$ (Table 12). This indicates that the presence of methoxyl groups at C-4 and C-7 in **15** determines that the most stable conformer possesses H-1 and H-3 in *pseudoequatorial* position and H-2 in *equatorial*, avoiding the $A^{1,3}$ *strain*, as informed for the *γ*-diasarone. On the other hand, the differences of the chemical shifts observed in H-1 and C-1 in the two cycloadducts show that indane **15** does not present the *Asarone effect* due to the absence of the methoxyl group in C-2′. Instead, this effect is observed in cycloadducts **16** and **17**.

Table 12. ^{1}H-NMR spectral data of the aliphatic carbon atoms of 1-aryl-3-ethyl-2-methylindanes: diastereomers *γ*

Compound	H-1	H-2	H-3	CH_3	$J_{1,2}$	$J_{2,3}$
γ-Diisosafrole	3.57	1.99	2.65	1.14	9.3	9.3
γ-Diasarone	4.30	2.08	2.69	1.18	4.1	4.1
13	3.55	2.02	2.67	1.12	9.4	9.4
14	**4.27**	2.07	2.65	1.17	**4.3**	**4.2**
15	3.88	2.12	2.75	1.19	**5.3**	**5.5**
16	**4.23**	2.05	2.65	1.15	8.6	8.1
17	**4.19**	2.10	2.67	1.16	9.0	9.0

Table 13. ^{13}C-NMR spectral data of the aliphatic carbon atoms of 1-aryl-3-ethyl-2-methylindanes: diastereomers *γ*

Compound	C-1	C-2	C-3	CH_3
γ-Diisosafrole	58.5	51.4	50.8	17.4
γ-Diasarone	**49.8**	47.6	52.3	22.0
13	58.37	51.25	50.8	17.28
1415	**49.91**	47.73	52.4	22.01
	57.49	49.66	52.9	22.04
16	**51.54**	51.03	50.8	18.97
17	**50.80**	50.75	50.4	18.65

NMR spectral analysis of 1-aryltetralins

Natural bisnorlignans, pachypostaudins A and B[9] (**18** and **19**), derived from cyclodimerization of 2,4,5-trimethoxyestyrene (Scheme 2), have a methoxyl group at C-8 and C-2′ in their structures. It is therefore interesting to study if the size of the non-aromatic ring and the substitution pattern in the tetralinic structures have the same influence as those observed in NMR

Table 14. ^{1}H-NMR and ^{13}C-NMR spectral data of the hydrogen and aliphatic carbon atoms of tetralinic structures

Compound	*δ*H-1	$J_{1,2}$	*δ*C-1	*δ*C-2	*δ*C-3	*δ*C-4
20[17,18]	2.73	m	**29.3**	23.3	23.3	29.3
21[19]	2.74	m	**25,9**	22.9	23.5	30.2
22[17,20]	2.75	6.1 (t)	**22.9**	22.9	23.1	29.7
23[21]	4.12	6.4	45.6	29.8	21.0	33.3
24[12]	4.07	6.0(t)	44.5	29.7	20.9	33.3
25[22]	4.44	6.8	**42.2**	30.1	26.9	33.5
26	4.52	7.0 (t)	**37.52**	29.83	20.62	30.62
27	4.41	**3.4** (**t**)	**38.54**	31.17	16.84	23.45
28	**4.66**	**3.2** (**d**)	**31.46**	28.20	17.13	23.51
18[9]	**4.78**	**4.8** (**m**)	**31.9**	29.1	17.5	22.9
29[23]	4.28	8.7 (t)	43.9	32.0	—	—
19[9]	**4.90**	**2.8** (**dd**)	**28.4**	29.8	121.2	123.5

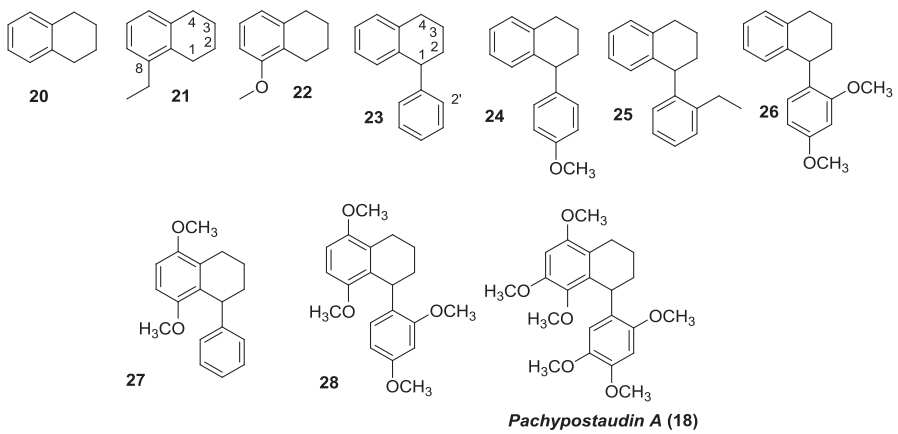


Figure 10. Synthetic and natural 1-aryltetralins.

Copyright © 2016 John Wiley & Sons, Ltd.

spectra for the indanic structures. The *Asarone effect* and the $A^{1,3}$ *strain* were analysed on the basis of the tetralinic structures shown in Fig. 10, and the NMR data are summarized in Table 14.

The NMR analysis of **21** and **22** compared with that of **20** shows that the ethyl and the methoxyl groups attached at C-8 present a shielding effect on C-1 ($\Delta\delta_C$ ~3 and 7 p.p.m.) due to steric and stereoelectronic factors respectively. In 1-aryltetralins, the presence of these groups attached at C-2′ has an effect on C-1 and H-1 similar to that shown in compounds **25** and **26** compared with **23** and **24** respectively ($\Delta\delta_C$ ~3 and 7 p.p.m. and $\Delta\delta_H$ ~0.3 and 0.5 p.p.m.). Tetralin **27**, which has a methoxyl group at C-8, presents a marked decrease in $J_{1,2}$ and a shielding effect in carbons sp^3 due to a conformational change regarding the monosubstituted tetralins analysed before, in which the aryl group is located in a *pseudoaxial* position to avoid the $A^{1,3}$ *strain*. The chemical shift of C-1, H-1 and $J_{1,2}$ of compound **28** clearly shows the *Asarone effect* and the $A^{1,3}$ *strain* as in the natural bisnorlignan pachypostaudin **18**.

The NMR spectra of **29** and pachypostaudin B (**19**) were identically analysed to assess the effects on this kind of dihydronaphthalene (Fig. 11 and Table 14).

The NMR data of H-1 and C-1 (δ_H and $J_{1,2}$) of the natural product **19** (δ_H 4.90 p.p.m.; $J_{1,2}$ 2.8 Hz and δ_C 28.4 p.p.m.) compared with the corresponding **29** (δ_H 4.28 p.p.m.; $J_{1,2}$ 8.7 Hz and δ_C 43.9 p.p.m.) show the same effects as those discussed in the preceding texts and that, in this case, the sp^2 carbons do not exert appreciable influence.

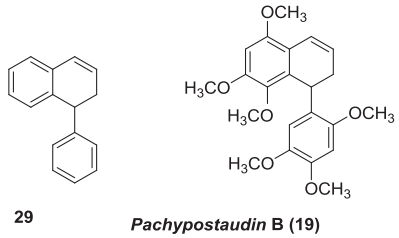


Figure 11. Synthetic and natural 1-aryldihydronaphthalenes.

Figure 12. Natural stilbenes.

NMR spectral analysis of 1,2,3-triaryltetralinic structures

Natural tetralinic cyclodimers with hydroxyl groups and/or methoxyl groups and whose biosynthetic origin are stilbene, resveratrol, oxyresveratrol and isorhapontigenin (Fig. 12) have attracted strong interest for their antioxidant properties in the preservation of fruits and durability of wood.[8]

Tetralins derived from these natural stilbenes have hydroxyl or methoxyl groups at C-8 and C-2′, as is the case of bisnorlignans

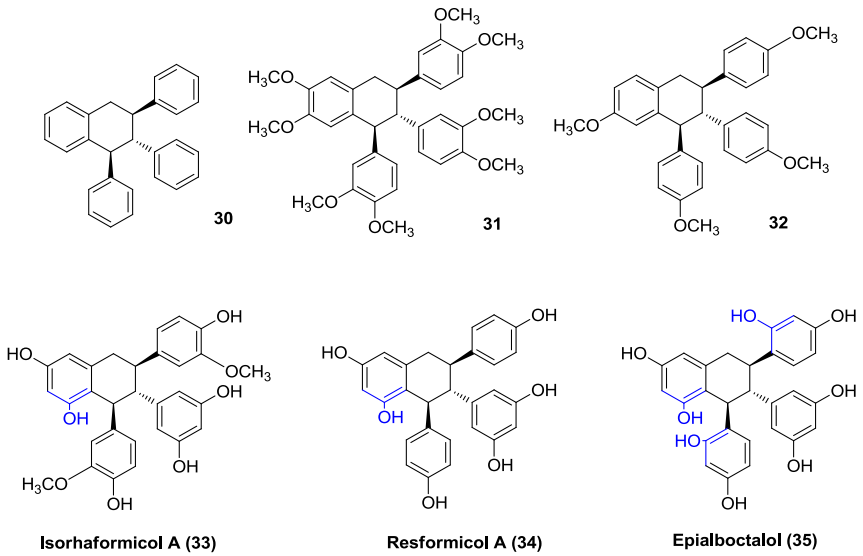


Figure 13. Synthetic and natural 1,2-*trans*-2,3-*trans*-1,2,3-triaryltetralins: diastereomer γ.

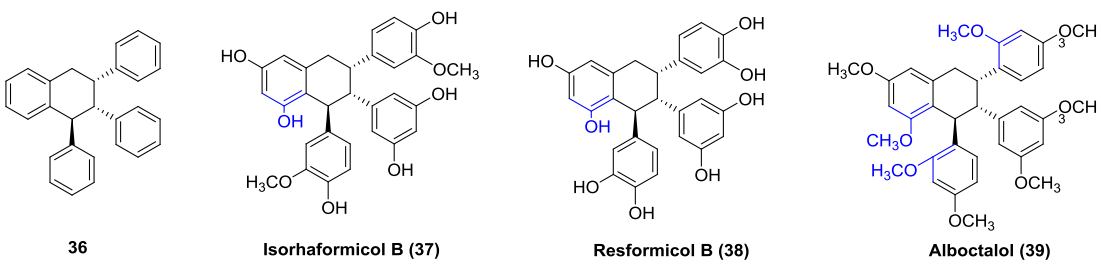


Figure 14. Synthetic and natural 1,2-*trans*-2,3-*cis*-1,2,3-triaryltetralins: diastereomer α.

Copyright © 2016 John Wiley & Sons, Ltd.

18 and **19**. This substitution pattern is of interest for a comparative analysis of ^{1}H-NMR and ^{13}C-NMR spectra of 1,2,3-triarylsubstituted tetralins, which do not have substituents at those positions. In this study, synthetic tetralins (**31**–**32** and **36**) and natural tetralins: isorhaformicol A (**33**),[8] resformicol A (**34**),[25] epialboctalol (**35**),[8] isorhaformicol B (**37**),[8] resformicol B (**38**),[8] alboctalol (**39**) [24] and restrytisol C (**40**)[26] were used (Figs 13 and 14).

Synthetic compounds **30**–**32** are diastereomers γ (1,2-*trans*-2,3-*trans*) that do not have substituents at C-8 and C-2′ unlike **33**–**35**. The NMR data of the latter three show $A^{1,3}$ *strain* due to the decrease in $J_{1,2}$ and smaller chemical shift of H-1 and C-1, as observed in tetralins **27**. Besides, compound **35** presents *Asarone effect* on H-1 and C-1 and on H-3 and C-3 due to the hydroxyl group at C-2′ of the aryl groups attached at C-1 and C-3 (Table 15).

The comparative analysis of the NMR spectroscopic data of diastereomer α (1,2-*trans*-2,3-*cis*) **36** regarding **37**–**39** (Fig. 14 and Table 16), which have substituents at C-8 or C-8 and C-2′ (hydroxyl or methoxyl group), shows effects similar to those observed in diastereomers γ (Fig. 13).

Lastly, the NMR spectra of restrytisol C (**40**), a natural dihydronaphthalene produced by grapes (*Vitis* spp)[26] compared with **41**, show values that indicate that the trisubstituted ring adopts a conformation that avoids the $A^{1,3}$ *strain* due to the presence of the hydroxy group attached at C-8. In the dihydronaphthalene **42**, the *Asarone effect* is observed at H-2 and C-2 (Fig. 15 and Table 17). However, the presence of four sp^2 carbons in the triarylsubstituted cycle does not show the same trends as in the monosubstituted dihydronaphthalenes and triarylsubstituted tetralins.

Table 15. ^{1}H-NMR and ^{13}C-NMR spectral data of the hydrogen and aliphatic carbon atoms of 1,2,3-triarylsubstituted tetralins: diastereomer γ

Compound	δH-1	δH-3	$J_{1,2}$	δC-1	δC-2	δC-3	δC-4
30	4.25	3.25	10.5 (d)	55.39	56.19	46.82	40.04
31	4.16	3.36	10.3 (d)	54.1	55.4	45.8	38.9
32	4.19	3.37	10.3(d)	54.4	55.0	45.4	39.0
33 Isorhaformicol A	**4.23**	3.01	**8.1 (d)**	**50.3**	59.9	48.0	41.0
34 Resformicol A	**4.26**	3.04	**6.9 (d)**	**49.8**	60.0	47.9	41.0
35 Epialboctalol	**4.42**	**3.51**	**8.2 (d)**	**44.1**	56.2	**40.3**	40.1

Table 17. ^{1}H-NMR and ^{13}C-NMR spectral data of the hydrogen and aliphatic carbon atoms of *trans*-1,2,3-triarylsubstituted dihydronaphthalenes

Compound	δH-1	δH-2	$J_{1,2}$	δC-1	δC-2
40 *Restrytisol C*	4.62	4.79	4.4 (d)	54.0	49.8
41[27]	4.12	4.12	(sa)	52.0	51.0
42[27]	4.20	4.78	(sa)	49.0	45.6

NMR spectral analysis of other indanic and tetralinic structures

In 1976, Deshpande *et al.*[28] assigned a 1,2-diaryl-2-benzylindane structure to alboctalol, the cyclodimer of oxyresveratrol, on the basis of spectroscopic data and biogenetic considerations, without indicating the stereochemistry (**43**). Later, the same researchers published the revised structure of alboctalol **39**[24] (Fig. 16).

With the aim of confirming the proposed structure and assigning the configuration, Alesso *et al.*[7] conducted the stereodirected synthesis of the frame of **43**. In an exploratory study, the two diastereomers of 1,2-diphenyl-2-benzylindane (**44a** and **44b**) were obtained, and then the respective octamethylderivatives of **43**[11] were synthesized (Fig. 17).

The ^{1}H-NMR and ^{13}C-NMR spectroscopic data of **44** and **45** (Table 18) are indicative of *Asarone effect* in positions 1 and 2 of diastereomers **45a** and **45b**. This effect is due to the 2,4-dimethoxyphenyl groups attached at C-1 and C-2 ($\delta_{H\text{-}1}$ 4.60 and 4.57 p.p.m. in **44a** and **44b** vs $\delta_{H\text{-}1}$ 4.94 and 4.93 p.p.m. in **45a** and **45b**), and the $\delta_{C\text{-}1}$ and $\delta_{C\text{-}2}$ show the consequent protection.

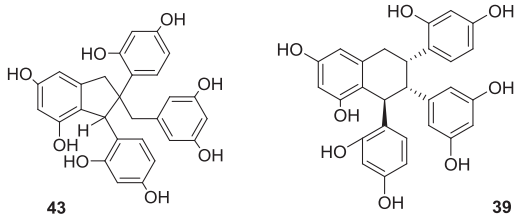


Figure 16. Proposed structures for alboctalol.

Table 16. ^{1}H-NMR and ^{13}C-NMR spectral data of the hydrogen and aliphatic carbon atoms of 1,2,3-triarylsubstituted tetralins: diastereomer α

Compound	δH-1	δH-3	$J_{1,2}$	δC-1	δC-2	δC-3	δC-4
36[13]	4.57	3.57	2.7(d)	50.11	54.59	39.37	30.60
37 Isorhaformicol B	4.42	3.32	Broad singlet (brs)	**45.9**	56.2	38.7	32.3
38 Resformicol B	4.36	3.23	(s)	**45.4**	56.4	37.3	31.4
39 Alboctalol	**4.84**	3.72	(s)	**37.9**	48.0	**31.0**	29.9

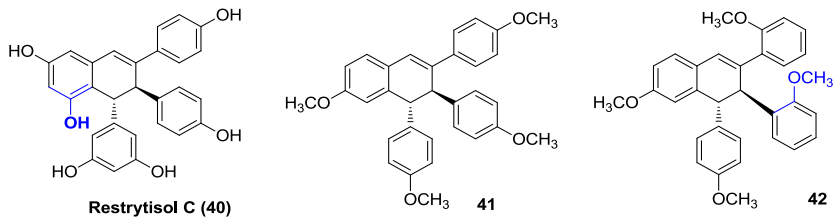


Figure 15. Synthetic and natural 1,2-*trans*-1,2,3-triaryldihydronaphthalenes.

Copyright © 2016 John Wiley & Sons, Ltd.

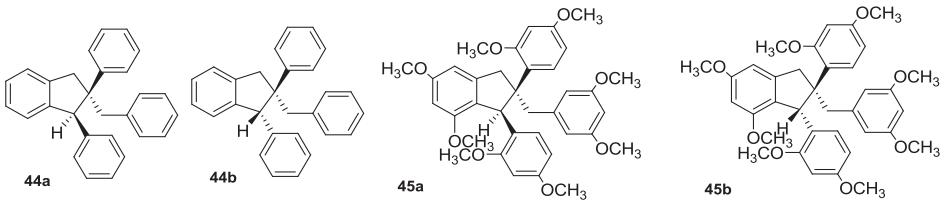


Figure 17. Synthetic 2-benzyl-1-diarylindanes.

Table 18. ^{1}H-NMR and ^{13}C-NMR spectral data of the hydrogen and aliphatic carbon atoms of 1,2-diaryl-2-benzylindanes

Compound	δH-1	δH-3	δCH$_2$Ph	δC-1	δC-2	δC-3	δCH$_2$Ph
44a	**4.60**	3.21/3.56	3.05/3.32	**63.2**	**57.7**	40.0	48.4
44b	4.57	3.20/3.36	2.62/2.97	64.2	57.3	39.3	43.0
45a	**4.94**	3.39/**	3.07/**	**60.5**	**55.9**	44.6	53.4
45b	4.93	3.20/3.33	2.62/3.02	60.6	56.0	41.6	44.9

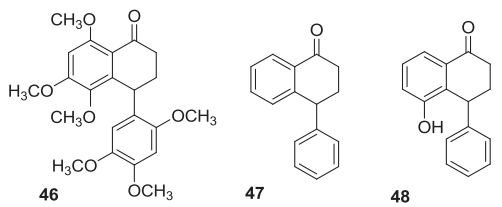


Figure 18. Synthetic and natural 1-aryltetralones.

Table 19. ^{1}H-NMR and ^{13}C-NMR spectral data of the hydrogen and aliphatic carbon atoms of 4-aryltetralones

Compound	δH-1	$J_{1,2}$	δC-1	δC-2	δC-3	δC-4
46[29]	**5.03**	(m)	**32.5**	**27.6**	**35.9**	197.6
47[30]	**4.31**	7.9, 4.6 (dd)	**45.6**	32.1	37.0	198.3
48[31]	**4.5–4.6**	(m)	**33.9**	31.0	38.4	198.5

Another example is the tetralone **46** isolated from *Peperomia pellucida*,[29] which shows the two effects discussed in this paper with reference to tetralones **47** and **48** (Fig. 18 and Table 19).

Conclusions

This study evaluated the effect exerted by the methoxyl groups at C-7 and C-2′ on the chemical shift of bibenzylic hydrogen and carbon atoms as well as on $J_{1,2}$ in indanic structures and was extended to tetralinic structures with methoxyl groups in C-8 and C-2′.

In both indanic and tetralinic structures, the presence of a methoxyl group at C-2′ produces a stereoelectronic effect that we called *Asarone effect*. The presence of a methoxyl group attached at C-7 in indanes or to C-8 in tetralins determines that the most favoured conformation for the pentagonal or hexagonal ring is the one that decreases the $A^{1,3}$ *strain* because the aryl group takes the pseudoaxial position.

These two effects, $A^{1,3}$ *strain* and *Asarone effect*, are significant and must be taken into account when using monodimensional NMR data for the configurational assignment of these structures, which are very common in products derived from natural styrenes and stilbenes.

Experimental

General

Nuclear magnetic resonance spectra were recorded on a 7.05 Tesla Criomagnet Bruker-Oxford BZH 300/89 with a resonance frequency of 300.130 MHz ^{1}H and ^{13}C 75.468 MHz. Probe multinuclear Z3150/0006 (5 mm). Data acquisition system and control Bruker Avance III. Administration and process software Bruker TOPSPIN 3.2, a 400.13-MHz ^{1}H and 100.61-MHz ^{13}C Ultra Shield NMR Spectrometer, a 500.13-MHz ^{1}H-NMR and 125.76-MHz ^{13}C-NMR Bruker and 14.1 Tesla magnet Bruker Ultra Shield with shim system BOSS II resonance frequency of 600.13 MHz ^{1}H and ^{13}C 150.91 MHz. Probe multinuclear Bruker SmartProbe BBFO (5 mm). Data acquisition system and control Bruker Avance III. Chemical shifts (δ) are quoted in parts per million and are reference to the residual solvent peak $CDCl_3$, δ = 7.28 p.p.m. (^{1}H), δ = 77.4 p.p.m. (^{13}C). Spin multiplicities as s, brs, d, dd, t, quadruplet (q) and m. Coupling constant (J) is given in Hz.

The HMBC spectra were measured with a pulse sequence hmbcgplpndqf (standard sequence pulse Bruker catalogue).

The HSQC spectra were measured with a pulse sequence hsqcgpph (standard sequence pulse Bruker catalogue).

Nuclear overhauser spectra were recorded on Bruker Ultra Shield spectrometer, operating at 600 MHz, with a spectral width of 10.013 p.p.m. (6.009615 kHz) in both F2 and F1 domains (TD F1: 2048, F2: 256 points), acquired with 16 scans per increment and relaxation delays of 1.0 s. The mixing time in NOESY experiments was 0.5 s. Data processing was performed on a 2 × 2 K data matrix.

Microanalyses were performed by Elemental Analyser Carlo Erba. Preparative thin-layer chromatography (p-TLC) was done on Merck Silica Gel 60 GF_{254}, and analytical TLC was performed on Merck aluminium sheets Silica Gel 60 GF_{254}. Commercial compounds were purchased from Aldrich Chemical Co. Tetrahydrofuran and CH_2Cl_2 were distilled from sodium/benzophenone and CaH_2 respectively. Melting points are uncorrected and were determined in a Thomas Hoover apparatus. In cases where synthetic intermediates or products were isolated by 'aqueous workup (aqueous solution, organic solvent)', the procedure was to quench the reaction mixture with the indicated aqueous solution, dilute with the indicated organic solvent, separate the organic layer, extract the aqueous layer several times with the organic solvent, dry the combined organic extracts over Na_2SO_4 and remove the solvent under reduced pressure (water aspirator) with a Büchi Rotavapor.

Copyright © 2016 John Wiley & Sons, Ltd.

General procedure for the formal [3 + 2] cycloaddition of an alcohol and an alkene in the presence of $SnCl_4$

*r-1-(4-Methoxyphenyl)-t-2-methyl-5,6-dimethoxyindane (**1**)*

(*E*)-4-methoxyphenyl-β-methylstyrene (0.07 g, 0.48 mmol) and $SnCl_4$ (0.156 g, 0.60 mmol) were sequentially added to a solution of (3,4-dimethoxyphenyl)methanol (0.108 g, 0.46 mmol) in CH_2Cl_2 (10 ml) at 0 °C. The resulting solution was stirred for 30 min at 0 °C and then poured into a rapidly stirred solution of $NaCO_3H$ 5%. Aqueous workup ($NaCO_3H$, CH_2Cl_2) followed by p-TLC (95 : 5, hexane/isopropanol) afforded 0.057 g (30%) of **1** (white solid), mp: 82–83 °C. ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.11 (d, *J* = 8.7, 2H, Ar), 6.87 (d, *J* = 8.7, 2H, Ar), 6.40 (s, 1H,Ar), 3.88 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 3.70 (d, *J* = 9.5, 1H, Ar*CH*Ar), 3.06 (dd, *J* = 7.4, 14.9 1H, *CH*$_2$Ar), 2.55 (dd, *J* = 9.5, 14.9, 1H, *CH*$_2$Ar), 2.35 (m, 1H, *CH*CH$_3$), 1.16 (d, *J* = 6.7, 3H, CH*CH*$_3$) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 158.22, 148.14, 148.01, 138.73, 136.46, 135.13, 129.48, 113.76, 108.04, 107.32, 58.85, 56.02, 55.91, 55.24, 46.87, 40.06, 18.32, p.p.m. Anal. Calcd. for $C_{19}H_{22}O_3$: C, 76.48, H, 7.43. Found: C, 76.50, H, 7.45.

*r-1-(4-Methoxyphenyl)-t-2-methyl-5,6,7-trimethoxyindane (**3**)*

General procedure was carried out with (3,4,5-trimethoxyphenyl) methanol (0.129 g, 0.66 mmol), (*E*)-4-methoxyphenyl-β-methylstyrene (0.097 g, 0.66 mmol) and $SnCl_4$ (0.23 g, 0.90 mmol). p-TLC (70 : 30, hexane/ethylacetate) afforded 0.14 g (65%) of **3** (clear oil). ^{1}H-NMR (600.13 MHz, $CDCl_3$) δ = 7.08 (d, *J* = 8.6, 2H, Ar), 6.84 (d, *J* = 8.6, 2H, Ar), 6.61 (s, 1H, Ar), 3.88 (s, 3H, OCH_3), 3.37 (d, *J* = *4.7*, 1H, CHAr), 3.81 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.40 (s, 3H, OCH_3), 3.19 (dd, *J* = 7.7, 15.6, 1H, CH_2), 2.52 (dd, *J* = 6.7, 15.6, 1H, CH_2), 2.39 (m, *J* = 6.8, 1H, *CH*CH$_3$), 1.17 (d, *J* = 6.8, 3H, CH_3) p.p.m. ^{13}C-NMR (150.91 MHz, $CDCl_3$) δ = 157.86, 153.29, 150.38, 140.83, 139.08, 137.82, 130.70, 128.43, 113.52, 103.44, 60.87, 60.05, 56.98, 56.11, 55.21, 45.27, 40.48, 19.99 p.p.m. Anal. Calcd. for $C_{20}H_{24}O_4$: C, 73.15, H, 7.37. Found: C, 73.18, H, 7.35.

*r-1-(2,4,5-Trimethoxyphenyl)-t-2-methyl-5,6,7-trimethoxyindane (**4**)*

General procedure was carried out with (3,4,5-trimethoxyphenyl) methanol (0.129 g, 0.66 mmol), (*E*)-2,4,5-trimethoxyphenyl-β-methylstyrene (0.137 g, 0.66 mmol) and $SnCl_4$ (0.23 g, 0.90 mmol). p-TLC (70 : 30, hexane/ethylacetate) afforded 0.145 g (57%) of **4** (clear oil). ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 6.61 (s, 1H, Ar), 6.58 (s, 1H, Ar), 6.33 (s, 1H, Ar), 4.35 (d, *J* = 5.0, 1H, CHAr), 3.89 (s, 3H, OCH_3), 3.88 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3), 3.49 (s, 3H, OCH_3), 3.13 (dd, *J* = 8.0, 15.6, 1H, CH_2), 2.47 (dd, *J* = 5.3, 15.6, 1H, CH_2), 2.35 (m, 1H, $CHCH_3$), 1.16 (d, *J* = 6.8, 3H, CH_3) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 158.76, 152.08, 150.56, 145.99, 145.28, 140.16, 136.74, 126.40, 126.30, 113.28, 105.58, 99.48, 60.81, 60.56, 57.91, 56.13, 56.10, 55.83, 53.61, 42.33, 40.84, 19.80 p.p.m. Anal. Calcd. for $C_{22}H_{28}O_6$: C, 68.02, H, 7.27. Found: C, 68.01, H, 7.25.

*t-3-Ethyl-t-2-methyl-r-1-(2-methoxyphenyl)-5,6-dimethoxyindane (**6**)*

General procedure was carried out with 1-(3,4-dimethoxyphenyl) propan-1-ol (0.098 g, 0.5 mmol), (*E*)-2-methoxyphenyl-β-methylstyrene (0.074 g, 0.50 mmol) and $SnCl_4$ (0.166 g, 0.64 mmol). p-TLC (CH_2Cl_2) afforded 0.090 g (55%) of **6** (clear oil). ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.16 (dt, *J* = 1.6, 8.2, 1H, Ar), 6.90 (d, *J* = 8.2, 1H, Ar), 6.76 (s, 1H, Ar), 6.74 (m, 2H, Ar), 6.48 (s, 1H, Ar), 4.33 (d, *J* = 6.7, 1H, *CH*-Ar), 3.87 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.72 (s, 3H, OCH_3), 2.90 (m, 1H, *CH*-CH_2CH_3), 2.44 (m, *J* = 6.7, 7.2, 7.9, 1H, *CH*-CH_3), 1.59 (m, 2H, CH_2), 0.99 (d, *J* = 7.2, 3H, CH-*CH*$_3$), 0.95 (t, *J* = 7.4, 3H, CH_2-*CH*$_3$) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 158.54, 148.68, 148.36, 140.22, 138.16, 133.62, 128.81, 127.71, 121.15, 110.89, 109.09, 108.39, 56.64, 56.62, 56.18, 50.33, 48.64, 48.23, 22.61, 15.09, 13.05 p.p.m. Anal. Calcd. for $C_{21}H_{26}O_3$: C, 77.27, H, 8.03. Found: C, 77.31, H, 7.95.

*t-3-Ethyl-t-2-methyl-r-1-(2-methoxyphenyl)-5,6,7-trimethoxyindane (**11**)*

General procedure was carried out with 1-(3,4,5-trimethoxyphenyl) propan-1-ol (0.113 g, 0.5 mmol), (*E*)-2-methoxyphenyl-β-methylstyrene (0.074 g, 0.50 mmol) and $SnCl_4$ (0.166 g, 0.64 mmol). p-TLC (CH_2Cl_2) afforded 0.093 g (53%) of **11** (clear oil). ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.13 (t, *J* = 7.4, 1H, Ar), 6.86 (d, *J* = 8.2, 1H, Ar), 6.72 (t, *J* = 7.4, 1H, Ar), 6.54 (s, 1H, Ar), 6.52 (d, *J* = 7.4, 1H, Ar), 4.36 (d, *J* = 2.5, 1H, *CH*-Ar), 3.88 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 2.91 (m, 1H, *CH*-CH_2CH_3), 2.35 (m, *J* = 2.5, 6.9, 7.4, 1H, *CH*-CH_3), 1.72 (m, 1H, CH_2), 1.46 (m, 1H, CH_2), 0.96 (d, *J* = 7.2, 3H, CH-*CH*$_3$), 0.91 (t, *J* = 7.4, 3H, CH_2-*CH*$_3$) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 157.95, 153.76, 151.07, 143.96, 133.54, 129.61, 129.48, 127.82, 127.60, 120.72, 110.84, 103.54, 61.56, 60.86, 56.80, 56.16, 49.12, 48.07, 46.14, 21.97, 15.66, 13.05 p.p.m. Anal. Calcd. for $C_{22}H_{28}O_4$: C, 74.13, H, 7.92. Found: C, 74.35, H, 7.80.

*c-3-Ethyl-t-2-methyl-r-1-(2,4,5-trimethoxyphenyl)-5,6-methylenedioxyindane (**17**)*

General procedure was carried out with 1-(3,4-methylenedioxyphenyl)propan-1-ol (0.09 g, 0.5 mmol), (*E*)-2,4,5-trimethoxyphenyl-β-methylstyrene (0.104 g, 0.50 mmol) and $SnCl_4$ (0.169 g, 0.65 mmol). p-TLC (80 : 20, hexane/ethylacetate) afforded 0.018 g (10%) of **17** (clear oil). ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 6.72 (s, 1H, Ar), 6.59 (s, 1H, Ar), 6.56 (s, 1H, Ar), 6.33 (s, 1H, Ar), 5.93 (d, *J*: 1.5, 1H, OCH_2O), 5.89 (d, *J*: 1.5, 1H, OCH_2O), 4.19 (d, *J* = 9.0, 1H, *CH*-Ar), 3.93 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 2.67 (m, *J* = 5.3, 5.8, 9.0, 1H, *CH*-CH_2), 2.10 (m, 1H, *CH*-CH_3), 1.85 (m, 2H, CH_2CH_3), 1.16 (d, *J* = 6.8, 3H, CH-*CH*$_3$), 0.99 (t, *J* = 7.4, 3H, CH_2-*CH*$_3$), p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 152.98, 148.51, 147.02, 146.93, 143.92, 142.31, 140.27, 124.97, 113.29, 105.64, 104.46, 100.89, 98.45, 57.51, 57.01, 56.23, 50.80, 50.75, 50.43, 25.57, 18.65, 11.47 p.p.m. Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.33, H, 7.07. Found: C, 71.12, H, 7.10.

General procedure for obtained 1-aryltetralins

*1-(2,4-Dimethoxyphenyl)-1,2,3,4-tetrahydronaphthalene (**26**)*

A solution of 2,4-dimethoxy bromobenzene (1.4 ml, 9.16 mmol) and 1,2-dibromoethane (0.76 ml, 9.16 mmol) in dry ether (10 ml) was added dropwise over a period of 5 h to magnesium turnings (474 mg, 19.75 mmol) under refluxing conditions, then the mixture was cooled to room temperature. A solution of 1-tetralone (250 mg, 1.86 mmol) in dry benzene (15 ml) was added dropwise during 35 min. The mixture was stirred for 4 h at reflux. After cooling at room temperature, the mixture was hydrolysed with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with chloroform (2 × 20 ml). Then, the organic extracts were dried and the solvent evaporated *in vacuo*. p-TLC (80 : 20, hexane/ethyl acetate) afforded 0.343 g (65%; clear oil) 1-(2,4-dimethoxyphenyl)-1,2,3,4-tetrahydronaphthalen-1-ol. ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.33 (m, 1H, Ar), 7.19 (m, 3H, Ar), 6.70 (d, *J* = 8.5, 1H, Ar), 6.51 (d, *J* = 2.4, 1H, Ar), 6.36 (dd, *J* = 2.4, 8.5, 1H, Ar), 3.79 (s, 6H, OCH_3), 4.16 (s, 1H, OH), 2.84 (m, 2H, CH_2), 2.48 (ddd, *J* = 2.8, 8.8, 12.7, 1H, CH_2), 2.07 (ddd, *J* = 2.8, 10.1,

Copyright © 2016 John Wiley & Sons, Ltd.

12.9, 1H, CH_2), 1.89 (m, 1H, CH_2), 1.61 (m, 1H, CH_2), p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 159.81, 157.33, 141.53, 137.41, 130.12, 128.37, 128.21, 127.01, 126.07, 124.87, 103.39, 99.61, 75.58, 55.43, 55.31, 38.05, 29.64, 20.08 p.p.m. Anal. Calcd. for $C_{18}H_{20}O_3$: C, 76.03, H, 7.09. Found: C, 76.1, H, 7.10. A mixture of 1-(2,4-dimethoxyphenyl)-1,2,3,4-tetrahydronaphthalen-1-ol 63.4 mg, (0.22 mmol) in $CHCl_3$ (1 ml) and powdered sodium borohydride 83.3 mg (19 mmol) was added in portions over 2 min to trifluoroacetic acid (TFA; 1.33 ml) in a 50-ml three-neck flask at 0° under of nitrogen with vigorous stirring. After stirring the mixture for 5 min at 0°, the bulk of the TFA was removed *in vacuo* and the residue was treated with ice water (5 ml) and then 30% aqueous sodium hydroxide solution and extracted with 20-ml $CHCl_3$. The extracted was washed with water, dried over sodium sulfate and evaporated *in vacuo* to provide 73.55 mg (78%) of **26**. ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.14 (m, 2H, Ar), 7.06 (m, 1H, Ar), 6.88 (d, *J* = 7.6, 1H, Ar), 6.65 (d, *J* = 8.4, 1H, Ar), 6.52 (d, *J* = 2.4, 1H, Ar), 6.38 (dd, *J* = 2.4, 8.4, 1H, Ar), 4.50 (t, *J* = 6.0, 1H, CH-Ar), 3.86 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.88 (m, 2H, CH_2), 2.05 (m, 1H, CH_2), 1.88 (m, 2H, CH_2) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 158.93, 157.84, 139.97, 137.97, 130.55, 130.06, 128.83, 128.30, 125.57, 125.54, 103.71, 98.34, 55.45, 55.29, 37.52, 30.62, 29.83, 20.62 p.p.m. Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.56, H, 7.51. Found: C, 80.55, H, 7.50.

*5,8-Dimethoxy-1-phenyl-1,2,3,4-tetrahydronaphthalene (**27**)*

General procedure was carried out with bromobenzene (0.2 ml, 1.95 mmol), magnesium turnings (47.0 mg, 1.95 mmol) and 5,8-dimetethoxy-1-tetralone (80.0 mg, 0.39 mmol). p-TLC (80 : 20, hexane/ethylacetate) afforded 0.067 g (61%) of 5,8-dimethoxy-1-phenyl-1,2,3,4-tetrahydronaphthalen-1-ol (clear oil). ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.38 (m, 1H, Ar), 7.24 (m, 4H, Ar), 6.74 (d, *J* = 8.8, 1H, Ar), 6.72 (d, *J* = 8.8, 1H, Ar), 4.80 (s, 1H, OH), 3.85 (s, 3H, OCH_3), 3.48 (s, 3H, OCH_3), 2.85 (td, *J* = 4.4, 4.4, 17.7, 1H, CH_2), 2.67 (ddd, *J* = 5.7, 10.2, 17.7, 1H, CH_2), 2.20 (m, 1H, CH_2), 2.03 (m, 1H, CH_2), 1.77 (m, 1H, CH_2), 1.52 (m, 1H, CH_2) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 151.54, 150.25, 131.27, 128.67, 128.49, 127.57, 127.47, 126.54, 126.27, 125.66, 109.57, 108.70, 75.50, 55.93, 55.69, 40.36, 24.05, 18.59 p.p.m. Anal. Calcd. for $C_{19}H_{23}O_2$: C, 80.53; H, 8.18. Found: C, 80.51, H, 8.16. General procedure was carried out with 1.4 ml of TFA, 87.1 mg (2.3 mmol) of $NaBH_4$ and 67 mg (0.23 mmol) of 5,8-dimethoxy-1-phenyl-1,2,3,4-tetrahydronaphthalen-1-ol. p-TLC (80 : 20, hexane/ethyl acetate) afforded 0.34 g (54%; clear oil) of **27**. ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.23 (t, *J* = 7.1, 2H, Ar), 7.14 (t, *J* = 7.1, 1H, Ar), 7.00 (d, *J* = 7.1, 1H, Ar), 6.73 (d, *J* = 8.7, 1H, Ar), 6.64 (d, *J* = 8.7, 1H, Ar), 4.41 (t, *J* = 4.3, 1H, C*H*-Ar), 3.85 (s, 3H, OCH_3), 3.83 (s, 3H, OCH_3), 2.90 (td, *J* = 1.9, 5.5, 17.6, 1H, CH_2), 2.55 (ddd, *J* = 4.4, 6.7, 17.6, 1H, CH_2), 1.98 (m, 2H, CH_2), 1.63 (m, 2H,CH_2) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 151.62, 151.43, 147.23, 128.91, 128.17, 128.04, 127.66, 125.23, 107.84, 107.36, 55.92, 55.63, 38.54, 31.17, 23.45, 16.84 p.p.m. Anal. Calcd. for $C_{19}H_{23}O_2$: C, 80.53; H, 8.18. Found: C, 80.51, H, 8.16.

*1-(2,4-Dimethoxyphenyl)-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalene (**28**)*

General procedure was carried out with 2,4-dimethoxy bromobenzene (1.0 ml, 6.91 mmol), 1,2-dibromoethane (0.57 ml, 6.91 mmol) magnesium turnings (165.84 mg, 6.91 mmol) and 5,8-dimetethoxy-1-tetralone (0.25 mg, 1.21 mmol). p-TLC (80 : 20, hexane/ethylacetate) afforded 0.20 g (48%) of 1-(2,4-dimethoxyphenyl)-5,8-dimethoxy-1,2,3,4-tetrahydronaphthalene-1-ol (clear oil). ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.24 (d, *J* = 7.5, 1H, Ar), 6.72 (d, *J* = 8.8, 1H, Ar), 6.66 (d, *J* = 8.8, 1H, Ar), 6.45 (d, *J* = 2.1 Hz, 1H, Ar), 6.43 (dd, *J* = 2.1, 8.1, 1H, Ar), 3.82 (s, 3H, OCH_3), 4.33 (s, 1H, OH), 3.79 (s, 3H, OCH_3), 3.53 (s, 3H, OCH_3), 3.41 (s, 3H, OCH_3), 2.87 (td, *J* = 5.4, 5.5, 17.1 Hz, 1H, CH_2), 2.55 (ddd, *J* = 5.1, 8.4, 17.0, 1H, CH_2), 2.33 (m, 1H, CH_2), 2.02 (m, 1H, CH_2), 1.78 (m, 1H, CH_2), 1.66 (m, 1H, CH_2) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 159.28, 157.06, 151.74, 151.45, 132.68, 130.51, 128.84, 128.10, 109.81, 108.54, 103.59, 99.88, 73.82, 56.19, 55.91, 55.57, 55.24, 37.92, 24.05, 19.45 p.p.m. Anal. Calcd. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.73, H, 7.04. General procedure was carried out with 0.46 ml of TFA, 28.78 mg (0.76 mmol) of $NaBH_4$ and 26.3 mg (0.076 mmol) of 1-(2,4-dimethoxyphenyl)-5,8-dimethoxy-1,2,3,4-tetrahydro naphthalene-1-ol. p-TLC (80 : 20, hexane/ethyl acetate) afforded 0.0163 g (65%; clear oil) of **28**. ^{1}H-NMR (300.130 MHz, $CDCl_3$) δ = 7.14 (m, 2H, Ar), 7.06 (m, 1H, Ar), 6.88 (d, *J* = 7.6, 1H, Ar), 6.65 (d, *J* = 8.4, 1H, Ar), 6.52 (d, *J* = 2.4, 1H, Ar), 6.38 (dd, *J* = 2.4, 8.4, 1H, Ar), 4.50 (t, *J* = 6.0, 1H, CH-Ar), 3.86 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 2.88 (m, 2H, CH_2), 2.05 (m, 1H, CH_2), 1.88 (m, 3H, CH_2) p.p.m. ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 158.53, 157.40, 151.53, 151.36, 129.98, 129.83, 129.43, 128.48, 127.83, 107.85, 107.03, 102.86, 98.40, 56.19, 55.56, 55.55, 55.17, 31.46, 28.20, 23.51, 17.13 p.p.m. Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.56, H, 7.51. Found: C, 80.55, H, 7.50.

General procedure for obtained 1,2,3-triphenyltetralins

General procedure employed by Hiscock *et al.*[13] was carried out with *trans*-stilbene (1 g) and $SbCl_3$ (5 g). p-TLC (80 : 20, hexane/ethyl acetate) afforded 150 mg of **30** (mp: 113–115 °C) and 132 mg of **36** (mp: 144–146 °C).

*(1R/S,2R/S,3S/R)-1,2,3-triphenyl-1,2,3,4-tetrahydronaphthalene (**30**)*

Proton nuclear magnetic resonance (300.130 MHz, $CDCl_3$) δ = 7.25–6.85 (m, 19H, Ar), 4.42 (d, *J* = 10.7, H-1), 3.56 (ddd, *J* = 4.2, 10.9, 11.5, H-2), 3.43 (dd, *J* = 12.7, 16.0, H-4a), 3.40 (dd, *J* = 10.9, 11.1, H-3), 3.25 (dd, *J* = 4.0, 16.2, H-4b). ^{13}C-NMR (75.468 MHz, $CDCl_3$) δ = 145.40, 144.20, 142.56, 139.86, 136.84, 130.06, 129.32, 128.40, 128.25, 128.03, 127.92, 127.69, 127.59, 126.11, 125.91, 126.61, 56.19, 55.39, 46.82, 40.04.

*(1R/S,2R/S,3R/S)-1,2,3-Triphenyl-1,2,3,4-tetrahydronaphthalene (**36**)*

Proton nuclear magnetic resonance (500 MHz, $CDCl_3$) δ = 7.31–7.02 (m, 15H, Ar), 6.69 (dd, *J* = 2.0, 5.5, 2H, Ar), 6.58 (d, *J* = 7.0, 2H, Ar), 4.57 (d, *J* = 2.6, H-1), 3.57 (ddd, *J* = 2.8, 3.5, 9.9, H-3), 3.40 (t, *J* = 3.3, H-2), 3.08 (m, 2H, CH_2). ^{13}C-NMR (125 MHz, $CDCl_3$) δ = 147.76, 142.97, 141.32, 137.83, 137.56, 130.85, 129.10, 129.04, 128.95, 128.29, 128.20, 127.47, 126.36, 126.32, 126.26, 126.17, 126.08, 54.59, 50.11, 39.37, 30.60.

Acknowledgement

This study was supported by Universidad Nacional de Luján and Universidad de Buenos Aires.

References

[1] a) W. Baker, J. Enderby. *J. Chem. Soc.* **1940**, 1094–1098; b) A. Müller, M. Mészaros, K. Kormendy, A. Kusman. *J. Org. Chem.* **1952**, *17*, 787–799; c) J. M. van der Zandem, G. de Vries. *Rec. Trav. Chim.* **1952**, *71*, 733–739.
[2] J. MacMillan, I. L. Martin, D. J. Morris. *Tetrahedron* **1969**, *25*, 905–914.
[3] a) E. Al-Farhan, P. M. Keehn, R. Stevenson. *J. Chem. Research (S)* **1992**, 36–37; b) E. Wenkert, H. E. Gottlieb, O. R. Gottlieb, M. O. da S. Pereira, M. D. Formiga. *Phytochemistry* **1976**, *15*, 1547–1551; c) S. R. Angle, D. O. Arnaiz. *J. Org. Chem.* **1992**, *57*, 5937–5594.

Copyright © 2016 John Wiley & Sons, Ltd.

[4] a) A. Gonzalez de Castro, J. Xiao. *J. Am. Chem. Soc.* **2015**, *137*, 8206–8218; b) V. V. Kouznetsov, D. R. Merchan Arenas. *Tetrahedron Lett.* **2009**, *50*, 1546–1549.
[5] a) D. B. Saxena. *Phytochemistry* **1986**, *25*, 553–555; b) C. Lemini, J. J. Mandoki, R. A. Cruz-Almanza, R. Toscano. *Crys. Struct. Commun.* **1990**, *C46*(8), 1542–1545.
[6] E. N. Alesso, B. Lantaño, M. Erlich, M. R. Torviso, L. M. Finkielsztein, G. Y. Moltrasio, J. M. Aguirre, E. Brunet. *ARKIVOC* **2003**, *X*, 283–297.
[7] a) F. Marcuzzi, G. Melloni. *J. Chem. Research (M)* **1979**, 2287–2297. *J. Chem. Research (S)*, **1979**, 184–185; b) E. N. Alesso, D. G. Tombari, G. Y. Moltrasio Iglesias, J. M. Aguirre. *Can. J. Chem.* **1987**, *65*, 2568–2574; c) E. N. Alesso, D. G. Tombari, A. F. Ibañez, G. Y. Moltrasio Iglesias. *Can. J. Chem.* **1991**, *69*, 1166–1170; d) E. N. Alesso, G. Y. Moltrasio Iglesias, J. D. Mufato, J. M. Aguirre. *Aust. J. Chem.* **1992**, *45*, 1753–1758; e) E. N. Alesso, D. E. Bianchi, G. Y. Moltrasio Iglesias, M. Gonzalez Sierra, J. M. Aguirre. *Aust. J. Chem.* **1994**, *47*, 1237–1247; f) B. Lantaño, J. M. Aguirre, E. A. Ugliarolo, M. R. Torviso, N. Pomilio, G. Y. Moltrasio. *Tetrahedron* **2012**, *68*, 913–921.
[8] a) M. Royer, G. Herbette, V. Epavier, J. Beauchêne, B. Thibaut, D. Stien. *Phytochemistry* **2010**, *71*, 1708–1713; b) X.-M. Li, K.-S. Huang, M. Lin, L.-X. Zhou. *Tetrahedron* **2003**, *59*, 4405–4413; c) E. N. Alesso, M. Erlich, M. R. Torviso, L. M. Finkielstein, B. Lantaño, J. M. Aguirre, G. Y. Moltrasio, P. Vasquez, L. Pizzzio, C. Cáceres, M. Blanco, H. Thomas. *Synth. Comm.* **2002**, *32*, 3803–3812; d) J. M. Aguirre, E. N. Alesso, G. Y. Moltrasio Iglesias. *J. Chem. Soc., PerkinTrans. 1* **1999**, 1353–1858.
[9] B. T. Ngadjui, D. Lontsi, J. F. Ayafor, B. L. Sondengam. *Phytochemistry* **1989**, *28*, 231–234.
[10] a) B. Lantaño, J. M. Aguirre, L. M. Finfielsztein, E. N. Alesso, E. Brunet, G. Y. Moltrasio. *Synth. Comm.* **2004**, *34*, 625–641; b) B. Lantaño, J. M. Aguirre, E. A. Ugliarolo, M. L. Benegas, G. Y. Moltrasio. *Tetrahedron* **2008**, *64*, 4090–4102.
[11] E. N. Alesso, L. M. Finlielsztein, B. Lantaño, J. M. Aguirre, G. Y. Moltrasio Iglesias. *J. Chem. Research (M)*, **1999**, 1309–1319. *J. Chem. Research (S)*, **1999**, 302–303.
[12] Y.-P. Xiao, X.-Y. Liu, C.-M. Che. *J. Organomet. Chem.* **2009**, *694*, 494–501.
[13] M. Hiscock, G. B. Porter. *J. Chem. Soc. Perkin II* **1972**, 79–83.
[14] a) D. M. Grant, B. V. Cheney. *J. Am. Chem. Soc.* **1967**, *89*, 5315–5318; b) B. V. Cheney, D. M. Grant. *J. Am. Chem. Soc.* **1967**, *89*, 5319–5323.
[15] The name Asarone is used to refer to the 2,4,5-trimethoxyphenyl of the aryl moiety in natural β-methylestirenes.
[16] a) F. Johnson. *Chem. Rev.* **1968**, *68*, 375–392; b) R. W. Hoffmann. *Chem. Rev.* **1989**, *89*, 1841–1860.
[17] C. E. Browne, P. H. Ruehle, T. K. Dobbs, E. J. Eisenbraun. *Org. Magn. Resonance* **1979**, *12*, 553–556.
[18] F. Nador, F. Y. Moglie, C. Vitale, M. Yus, F. Alonso, G. Radivoy. *Tetrahedron* **2010**, *66*, 4318–4325.
[19] G. L. Thompson, W. E. Heyd, L. A. Paquette. J. Am. Chem. Soc. 1974, 96, 3177–3179. M. Adamczyk, D. S. Watt*J. Org. Chem.* **1984**, *49*, 4226–4237.
[20] Y. Yoshimi, A. Ishise, H. Oda, Y. Moriguchi, H. Kanezaki, Y. Nakaya, K. Katsuno, T. Itou, S. Inagaki, T. Morita, M. Hatanaka. *Tetrahedron Lett.* **2008**, *49*, 3400–3404.
[21] S. T. Bright, J. M. Coxon, P. J. Steel. *J. Org. Chem.* **1990**, *55*, 1338–1344.
[22] M. C. Carreño, M. González-López, A. Latorre, A. Urbano. *J. Org. Chem.* **2006**, *71*, 4956–4964.
[23] K. Maeda, E. J. Farrington, E. Galardon, B. D. John, J. M. Brown. *Adv. Synth. Catal.* **2002**, *344*, 104–109.
[24] R. B. Bates, S. Caldera, V. H. Deshpande, B. L. Malik, S. K. Paknikar. *J. Nat. Prod.* **1997**, *60*, 1041–1042.
[25] a) M. C. Davis, T. J. Groshens. *Tetrahedron Lett.* **2012**, *53*, 3521–3523; b) W. Li, P. Chen, Y. Yang, X. Liu, T. Dong. *Tetrahedron* **2016**, *72*, 210–215.
[26] R. H. Cichewicz, S. A. Kouzi, M. T. Hamann. *J. Nat. Prod.* **2000**, *63*, 29–33.
[27] F. J. Hong, Y. Y. Low, K. W. Chong, N. F. Thomas, T. S. Kam. *J. Org. Chem.* **2014**, *79*, 4528–4543.
[28] V. H. Deshpande, P. V. Wakharkar, A. V. Rama Rao. *Indian J. Chem.* **1976**, *14B*, 647–650.
[29] S. Xu, N. Li, M.-M. Ning, C.-H. Zhou, Q.-R. Yang, M.-W. Wang. *J. Nat. Prod.* **2006**, *69*, 247–250.
[30] J. Yun, S. L. Buchwald. *J. Org. Chem.* **2000**, *65*, 767–774.
[31] K. Y. Koltunov. *Tetrahedron Lett.* **2008**, *49*, 3891–3894.

Copyright © 2016 John Wiley & Sons, Ltd.