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Lewis-acid-promoted reactions of 1-{[(2-methoxyethoxy)methoxy](tributylstannyl)methyl}cyclohexene

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Summary — As a model for a synthetic approach to taxol and taxotere, the condensation of racemic α-alkoxy allylic stannane **9** with aldehydes **10a–h** was examined. Under $BF_3{\cdot}OEt_2$-promoted reaction conditions, the ***syn-E* 11a–h** homoallylic alcohols were obtained as the major isomers. $EtAlCl_2$ was found to be an efficient promoter for the condensation of aldehyde **10e,f**. With β- or α-hydroxyaldehydes **10g** or **10h** in the presence of intramolecular chelated $MgBr_2$, the stereochemical outcome of the reaction was inverted to give, in high yield and good stereoselectivity, the ***anti-E* 11g,h** homoaldol products exhibiting the stereochemistry required for the synthesis of taxanes.

α-alkoxyallylic stannane / homoaldol reaction / homoallylic alcohol / Lewis-acid-promoted reaction / synthesis / taxol / taxotere

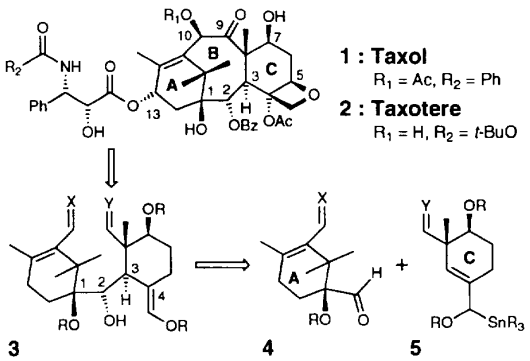
Résumé — Réactivité du 1-{[(2-méthoxyéthoxy)méthoxy](tributylstannyl)méthyl}cyclohexène en présence d'acid[illegible] de Lewis. En préliminaire à une nouvelle approche de la synthèse du taxol et du taxotère, la condensation de l'α-alcoxystannane allylique racémique **9** avec les aldéhydes **10a–h** a été étudiée. En présence de $BF_3{\cdot}OEt_2$, les alcools homoallyliques ***syn-E* 11a–h** sont les isomères majoritaires obtenus. Pour les aldéhydes **10e,f**, $EtAlCl_2$ s'est avéré le meilleur acide de Lewis. Lorsque les β- ou α-hydroxyaldéhydes **10g** ou **10h**, complexés de manière intramoléculaire par $MgBr_2$, sont condensés avec **11**, la stéréosélection de la réaction est inversée et les homoaldols ***anti-E* 11g,h** présentant la stéréochimie requise pour la synthèse des taxanes sont obtenus avec un excellent rendement et une bonne stéréosélectivité.

stannane α-alcoxyallylique / réaction d'homoaldolisation / alcool homoallylique / réaction en présence d'acides de Lewis / synthèse / taxol / taxotère

Paclitaxel (taxol®) **1** [1] and docetaxel **2** (taxotere®) [2] are two potent antitumor agents. Their unusual and interesting structure as well as their low natural availability have stimulated tremendous synthetic efforts from organic chemists, which have culminated in four total syntheses since 1994 [3].

One of our strategies for the total synthesis of taxol and taxotere was based on the eight-membered B cycle ring closure of seco-taxane **3** at the C9-C10 (scheme 1) [4]. For the construction of such a seco-precursor, one of the reactions envisioned was a homoaldol reaction performed between the α-hydroxyaldehyde **4** and the α-alkoxy allylic stannane **5** [5] leading to the intermediate **3** which corresponds to an *anti* homoaldol adduct. Analogous homoaldol approaches using either aldehyde/endocyclic allylsilane [6] or dimethyl acetal/exocyclic allylsilane [7] condensations were recently explored to construct the same C2-C3 bond of the taxane skeleton.

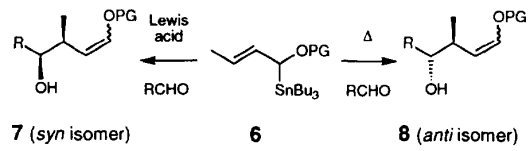
Both **7** (*syn* isomer) and **8** (*anti* isomer) homoallylic alcohols are accessible from condensation of (*E*) α-alkoxy crotylstannanes **6** [8] with aldehydes, depending on whether thermic [9] or Lewis acid conditions are used (scheme 2) [10].



Scheme 1

To our knowledge, no homoaldol reaction involving cyclic α-alkoxy allylic stannanes has been reported, except for intramolecular processes [11]. Moreover, although acid-promoted condensations of allylic stan-

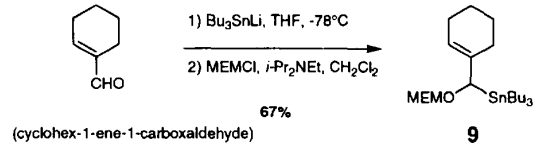
* Correspondence and reprints



Scheme 2

nanes with α- or β-alkoxyaldehydes conditions are well documented [12], the reactivity of α-alkoxy allylic stannanes with such aldehydes has not been reported.

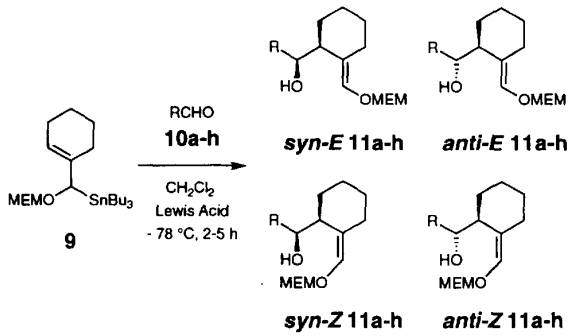
In order to ascertain the validity of our synthetic approach, we thus decided to study the reactivity of the 1-{[(2-methoxyethoxy)methoxy](tributylstannyl)methyl} cyclohexene **9** and the selectivity of its reactions with some representative aldehydes including α- or β-alkoxyaldehydes, in the presence of Lewis acids under non-chelating ($BF_3{\cdot}OEt_2$) or chelating ($MgBr_2$) conditions [13]. The required α-alkoxystannane **9** was prepared in good yield by addition of tributylstannyllithium (generated from hexabutyldistannane) on cyclohex-1-ene-1-carboxaldehyde, followed by protection of the hydroxyl function (scheme 3).



Scheme 3

$BF_3{\cdot}OEt_2$- or $EtAlCl_2$-promoted homoaldol reaction of 9: *syn* selectivity

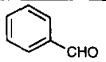
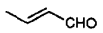
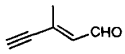
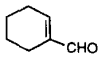
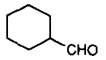
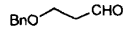
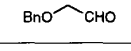
Preliminary studies have shown that $BF_3{\cdot}OEt_2$ was the most efficient promoter of the title reaction when non-hydroxylated aldehydes **10a–f** were condensed on α-alkoxy allylic stannane **9**. For example, $TiCl_4$ and $TiCl_2(O^iPr)_2$ totally destroyed **9** whereas $Ti(O^iPr)_4$ or $SnCl_4$ left this material unchanged. The results of the $BF_3{\cdot}OEt_2$-promoted reaction of **9** with aldehydes **10a–h** are summarized in scheme 4 and table I. All reactions were conducted at −78 °C in CH_2Cl_2 over 2–5 h until no more evolution occurred. After addition of saturated aqueous $NaHCO_3$ solution, the reaction mixtures were extracted with diethyl ether.



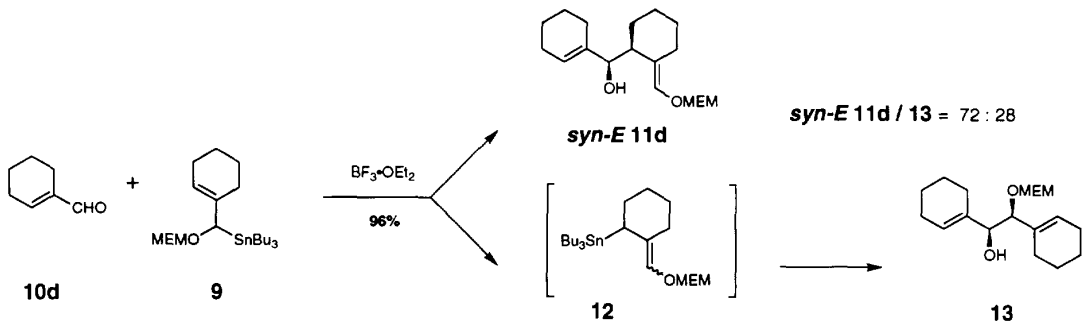
Scheme 4

With $BF_3{\cdot}OEt_2$, as expected, the major isomers obtained after reaction of α-alkoxy allylic stannane **9** with aldehydes **10a–h** were the ***syn-E* 11a–h** homoallylic alcohols. The yields were generally good (63–90%) and found optimal when 1.5 to 2.0 equiv of $BF_3{\cdot}OEt_2$ were used. However, when alkyl aldehydes such as 2-methylpropanal **10e** or cyclohexane-1-carboxaldehyde **10f** were treated with **9**, reactions did not occur in the presence of $BF_3{\cdot}OEt_2$ (entries 6 and 8); with $EtAlCl_2$, yields of 69 and 61% were obtained, the major isomers

Table I. Homoaldol reaction of **9** with aldehydes **10a–h**.

Entry	*RCHO*		*Equiv*	*Lewis acid (equiv)*	*Yield (%)*	*syn-E*[a]	*syn-Z*	*anti-E*	*anti-Z*
1		**10a**	1.1	$BF_3{\cdot}OEt_2$ (1.5)	84	83	0	6	11
2		**10a**	5.0	$EtAlCl_2$ (2.0)	95	63	16	7	14
3		**10b**	1.1	$BF_3{\cdot}OEt_2$ (1.5)	80	85	9	3	3
4		**10c**	1.1	$BF_3{\cdot}OEt_2$ (1.5)	63	90	–	10	–
5		**10d**	1.4	$BF_3{\cdot}OEt_2$ (1.5)	69	100[b]	0	0	0
6		**10e**	2.0	$BF_3{\cdot}OEt_2$ (2.0)	13[c]	–	–	–	–
7		**10e**	2.0	$EtAlCl_2$ (2.0)	69	73	2	23	2
8		**10f**	5.0	$BF_3{\cdot}OEt_2$ (2.0)	0	–	–	–	–
9		**10f**	5.0	$EtAlCl_2$ (2.0)	61	82	3	12	3
10		**10g**	1.5	$BF_3{\cdot}OEt_2$ (2.0)	70	80	6	8	6
11		**10h**	1.5	$BF_3{\cdot}OEt_2$ (2.0)	46	72	14	12	2

[a] Relative isomer ratio (%). [b] Along with 27% of **13**, see scheme 5. [c] The ratio of diastereomers was not determined.



Scheme 5

Table II. Coupling reactions of **10g** and **10h** with **9**.

Entry	*RCHO*		*T (°C)*	*t (h)*	*Yield (%)*	*anti-E/syn-E*
1	BnO⁄⁄CHO	**10g**	−20 to 20	3	94	80:20
2	BnO⁄⁄CHO	**10g**	−78	5	64[a]	96:04
3	BnO⁄⁄CHO	**10h**	−20 to 20	12	78	90:10

[a] Yield = 94% based on converted material (33% recovered starting material).

being again the ***syn-E* 11e,f** compounds (entries 7 and 9).

Treatment of cyclohexene-1-carboxaldehyde **10d** with 1.5 equiv of BF_3·OEt_2 afforded the *syn* 1,2-diol derivative **13** which was isolated as well as the major ***syn-E* 11d** homoaldol product (scheme 5). Formation of **13** could be explained by a preliminary transposition of the α-alkoxy allylic stannane **9** into the γ-stannyl enol ether **12** which subsequently underwent a nucleophilic addition on aldehyde **10d** [14]. The transposition of α-alkoxy allylic stannanes into γ-alkoxy allylic stannanes has been studied previously: preparation of a *syn* 1,2-diol according to such a route was initially described by Quintard et al [8b], and later observed by Marshall et al during the total synthesis of a ten-membered germacronolide (scheme 5) [15].

Reaction of β- and α-alkoxyaldehydes **10g** and **10h** proceeded in fair to good yields. In the case of **10g**, the homoaldol product **11g** was obtained in 70% yield as a 80:6:8:6 mixture of the *syn-E*, *syn-Z*, *anti-E* and *anti-Z* derivatives. The aldehyde **10h** gave a 72:14:12:2 mixture of the analogous **11h** isomers in 46% overall yield (entries 10 and 11).

The results obtained in the BF_3·OEt_2-promoted homoaldol reactions above appeared to be consistent with literature reports concerning related acyclic nucleophiles which lead to the formation of major *syn-E* homoallylic alcohols. In order to obtain the *anti-E* or *anti-Z* isomers required for our synthetic goal, we next turned to a $MgBr_2$-promoted homoaldol reaction.

$MgBr_2$·OEt_2-promoted homoaldol reactions of 9: *anti* selectivity

Coupling reactions of the β- or α-hydroxyaldehydes **10g** and **10h** with the α-alkoxy stannane **9** were found to be optimal with 3 equiv $MgBr_2$·OEt_2 (table II). Depending on the reaction time and temperature, the homoallylic alcohols **11g,h** were isolated in 78 to 96% yields with an *anti-E/syn-E* ratio of 80:20 to 96:4.

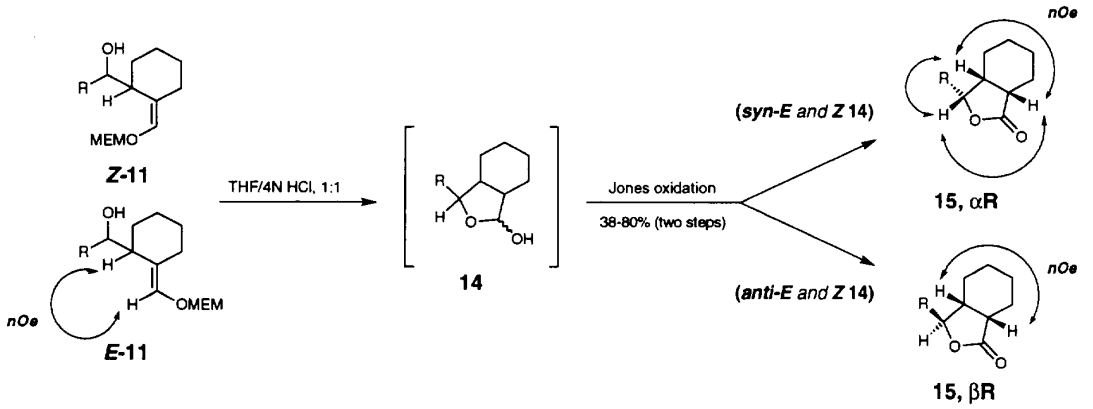
Stereochemical assignment

In order to establish unambiguously the *syn* or *anti* stereochemistry of the homoallylic alcohols **11a–h**, they were hydrolyzed to furnish the corresponding lactols **14a–h**, which were directly submitted to Jones' oxidation to give the γ-lactones **15a–h**. From NMR analysis, these γ-lactones were shown to possess a *cis* ring junction, and the *syn* or *anti* stereochemistry was deduced from the *cis* or *trans* relationship between the β-H and γ-H of the γ-lactone nucleus.

The enol ether double bond geometry of the homoaldol adducts **11a–h** was determined through ^1H NMR nOe experiments (scheme 6). The signals corresponding to the enol ether protons have been shown to be of diagnostic value to determine the ratio of homoaldol isomers.

Discussion

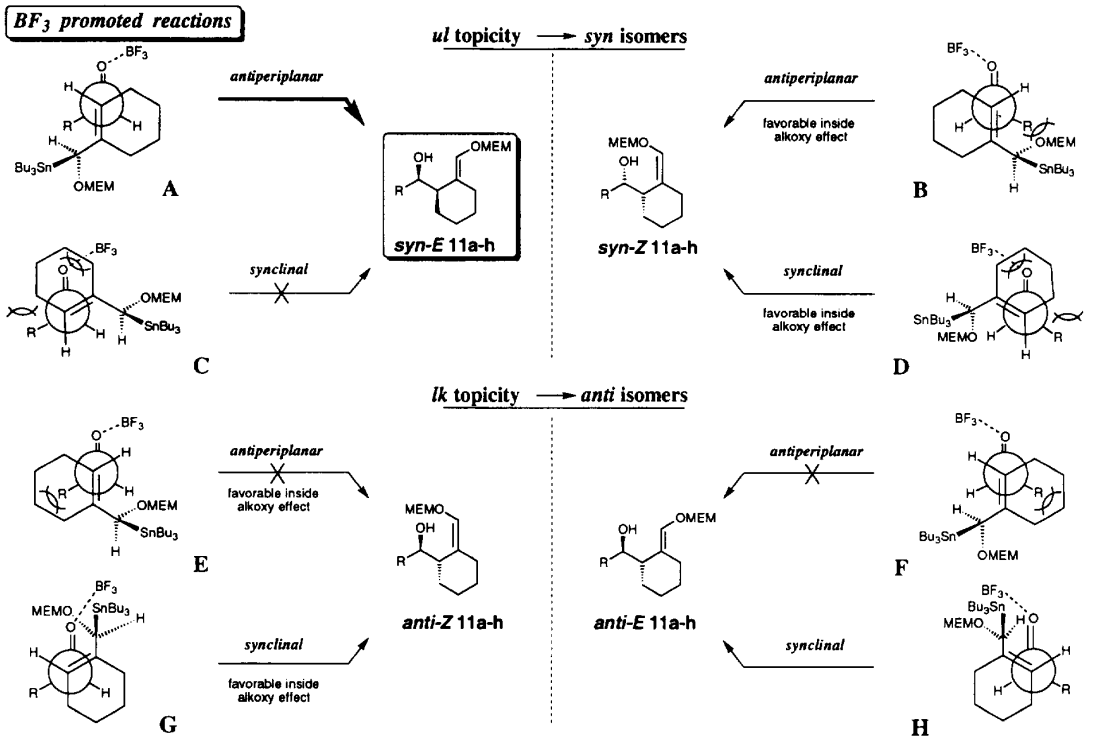
For homoaldol reactions promoted by the monodentate Lewis acid BF_3·OEt_2, acyclic antiperiplanar



Scheme 6

anti-S'_E transition states, initially proposed by Yamamoto et al for crotylstannanes [16], could reasonably account for the stereochemical bias favoring the formation of the major *syn* isomers (scheme 7). The transition states **A** or **B** can operate to give *syn-E* and *syn-Z* isomers, respectively. From a point of view of enantiopure compounds synthesis, it should be pointed out that **A** and **B** correspond to opposite diastereofacial selectivities leading to *pseudo*-enantiomeric *syn* homoallylic alcohols. High *syn-E/syn-Z* diastereofacial selectivities are observed whether olefinic, α- or β-alkoxy aldehydes or benzaldehyde are used.

These findings contrast with low diastereofacial selectivities observed with classical α-alkoxy crotylstannanes and are more in agreement with the excellent *syn-E* selectivities obtained by Gung et al with β-methyl-α-alkoxy crotylstannane [10c]. Surprisingly, these authors reported that no reaction occurred between this nucleophile and benzaldehyde, whereas with α-alkoxy crotylstannanes an inverse diastereofacial outcome of the reaction leading to *syn-Z* isomers is observed. It appears that the *syn* (for aromatic aldehydes) or *anti* (for aliphatic aldehydes) complexation of BF_3, which was used to explain these dramatic changes [17], does not operate in the case of the 1-(α-alkoxy stannylmethyl)cyclohexene **9** studied here. Gung attributed the low diastereofacial selectivities for α-alkoxy crotylstannanes to a subtle balance between steric effects and electronic inside alkoxy effects [18]. In agreement with the author's conclusions for β-methyl-α-alkoxy crotyl-



Scheme 7

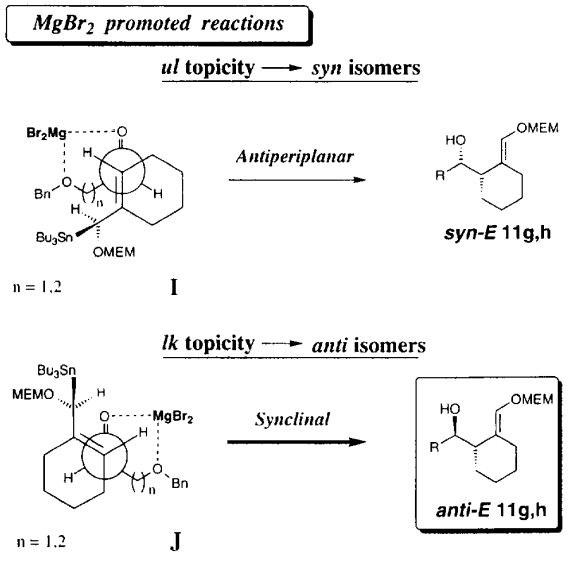
stannanes, the fact that transition state **B** (and also the most probable of the possible alternative synclinal transition state **D**), which is likely to give the minor *syn-Z* **11**, has favorable inside alkoxy effects, whereas **A**, which gives the major *syn-E* corresponding isomers, exhibits an outside alkoxy effect, clearly shows that the steric effects largely overcome the electronic effects in the BF_3-promoted reactions with the title nucleophile. This is not surprising considering traditional non-substituted crotyl tin chemistry especially if we recall that in the case of cyclohexene nucleophiles, the alkoxy electronic effects are expected to be diminished due to the donor ability of the cyclohexane methylene groups, an argument also claimed in the case of β-methyl-α-alkoxy crotylstannanes [18]. The lack of reactivity of the aldehydes **10d,e** may result from more marked steric interactions.

Moreover, for the formation of the *syn* isomers, alternative synclinal transition states **C** or **D** exhibiting the same *ul* topicity as **A** and **B** could be invoked, in agreement with literature propositions to explain the stereochemical outcome of analogous intramolecular [19] or intermolecular [20] reactions of allylstannanes. In **C** and **D**, the steric interactions mentioned for **B** are released and the only obvious difference involves a favorable inside alkoxy effect for **D**. However, a *gauche* steric interaction between R and a cyclohexene methylene as well as the novel eclipsing disposition between the C=O function and the cyclohexene ring appear to discredit these synclinal transition states.

The reason why in the case of α-sp^3-hybridized aldehydes **10d,e** $EtAlCl_2$ can promote the homoaldol reaction is still unclear, even if a Lewis acid metal with larger covalent radius can be reasonably claimed to release steric congestion preventing reaction between the two partners [21].

For the formation of the minor *anti* isomers, synclinal transition states with *lk* topicity must be invoked although the reasons leading to *E* or *Z* isomers here again seem to be very subtle. For obvious steric reasons, these *anti* isomers are not believed to be derived from *lk* antiperiplanar transition states **E** or **F** where the R moiety of the aldehyde and the cyclohexene ring must be eclipsed. Synclinal transition states **G** or **H** are probably preferred, **G** being favored by an inside alkoxy effect which is not present in **H**. However, in all cases tested except benzaldehyde, the *anti-E* isomers are slightly predominant over the *anti-Z* congeners, which seems to indicate that transition state **H**, which exhibits unfavorable outside alkoxy effect, prevails over **G**. This stereochemical bias is again in agreement with dominating steric interactions although more complex electrostatic or dipole interactions could be taken into account, especially in the case of aldehydes **10b** or **10g,h** [12a]. Thus, in analogous cases in which hydroxyaldehydes were condensed with allylstannanes, excess $BF_3{\cdot}OEt_2$, has already been claimed to promote chelation-controlled reactions [22]. By analogy with these literature precedents, the synclinal transition state **H** could account for increasing formation of ***anti-E* 11g,h** homoallylic alcohols, the major isomers produced when the reaction is promoted by $MgBr_2$ (see below).

The most striking feature arising from the present study is the inversion of the stereochemical outcome of the reaction when bidentate $MgBr_2$ is used instead of BF_3 in the presence of β- and α-hydroxyaldehydes **10g** and **10h**; ***anti-E* 11g,h** are produced with an excellent diastereoselectivity. These results are close to the anomalous *anti* stereoselectivity observed by Mikami et al during the condensation of β-substituted crotylstannanes with 2-(benzyloxy)propanal in the presence of $MgBr_2$ [23]. They are also reminiscent of *syn* versus *anti* selectivities observed by Marshall et al when (*E*)-γ-(methoxymethoxy)crotylstannanes are condensed with 2-(benzyloxy)propanal in the presence of BF_3 or $MgBr_2$ [24]. Scheme 8 shows the two most probable transition states **I** and **J** that would lead to *syn-E* or *anti-E* isomers respectively. In the antiperiplanar transition state **I** (corresponding to **A** for BF_3-promoted reactions) the steric interactions between the aldehydic chain and the MEMO residue are minimized whereas synclinal transition state **J** (corresponding to **H**) is favored owing to repulsive dipole–dipole interaction between OR and $BnO{\cdot}MgBr_2$. As already argued by the above authors to explain a preferred synclinal transition state of type **J** for similar chelated systems, one major stereochemical difference with the preceding BF_3-promoted reactions is that the Lewis acid is forced by the chelation in a *syn* direction with respect to the R residue of aldehyde. This disposition liberates some supplementary space *syn* to the aldehyde hydrogen, thus allowing the synclinal disposition of the bulky α-alkoxy stannylmethyl group. Such an argument should also be valuable when simple crotylstannanes are used as nucleophiles, a fact that has not been verified experimentally [25]. A common feature between Mikami's results and ours is the presence of a β-substituent on the allyltin chain. However, there is no obvious reason why **I** should be highly preferred over **J**: in agreement with Fleming's conclusions [23b], any explanation of the observed *anti-E* selectivity has to take into account a significant effect of these substituents.



Scheme 8

Conclusion

The α-alkoxy allylic stannane **9** was shown to react in good yield and high selectivity with aldehydes **10** in the presence of Lewis acids to give the corresponding homoallylic alcohols **11**. With BF_3-promoted reactions, the *syn* aldol products are obtained in good yields with a high predominance for the *syn-E* isomers, even in the case of aromatic aldehydes. The α-sp^3-hybridized aldehydes **10e,f** fail to react with BF_3 but give good results with $EtAlCl_2$. An inversion of the stereochemical outcome of the reaction is observed when $MgBr_2$ is used with α- or β-alkoxy aldehydes; the observed stereoselectivities are in good agreement with those already observed in the case (2-methylcrotyl)stannane nucleophiles [23]. Particularly interesting for our synthetic purposes is the result obtained with α-alkoxy aldehyde **10h** in the presence of $MgBr_2$ since the *anti* stereoselectivity is that required for taxoid synthesis. Current efforts are devoted to the application of these results to our initial synthetic project.

Experimental section

General methods

- *Physical data and spectroscopic measurements*

Melting points (mp) were determined on a Reichert apparatus and are uncorrected. Boiling points are uncorrected.

^{1}H NMR spectra were recorded on a Bruker WP 200 (200 MHz), or on a Bruker AM 400 (400 MHz) instrument. The solvent and the instrument are given for each product. The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.27 ppm). Data are reported as follows: δ, chemical shift; multiplicity (recorded as s, singlet; d, doublet; t, triplet; q, quartet; and m, multiplet), coupling constants (J in hertz), integration and assignment (aromatic, Ar). H,H-COSY and H,H-NOESY experiments were routinely carried out to ascertain H-H connectivities and configuration assignments, respectively. Italicized values refer to characteristic signals of diagnostic value for each isomer in a mixture.

^{13}C NMR spectra were recorded on the same instruments as above at 50.3 and 100.6 MHz respectively. The chemical shifts (δ) are expressed in ppm, reported from the central peak of deuterochloroform (77.14 ppm). J-modulated spin-echo technique (J-mod) experiments were used for evaluating CH multiplicities. When expressed, positive signals corresponding to CH_3 and CH are given as (+) and negative signals corresponding to CH_2 and quaternary C as (−). When necessary, ^{13}C spectra were assigned with the aid of HETCOR experiments. All italicized values refer to characteristic chemical shift.

Mass spectra (MS) were obtained on a Hewlett-Packard HP 5989B spectrometer via either direct introduction or GC/MS coupling with a Hewlett-Packard HP 5890 chromatograph. Ionization was obtained either by electronic impact (EI) or chemical ionization with ammonia (IC, NH_3) or methane (IC, CH_4). Mass spectral data are reported as m/z.

Infrared spectra (IR) were obtained on a Perkin-Elmer FT 1600 instrument using either NaCl salt plates (thin film) or NaCl cell (in the specified solvent) and are reported in terms of frequency of absorption (ν, cm^{-1}).

Microanalyses were performed by the Service de microanalyse, Institut de chimie des substances naturelles, CNRS, 91198, Gif-sur-Yvette, France.

- *Chromatography*

All reactions were monitored by thin-layer chromatography (TLC) carried out on E Merck Ref 5549 or 5554 precoated silica-gel 60F 254 plates. Visualization was accomplished with UV light then 7–10% ethanolic phosphomolybdic acid solution, anisaldehyde solution, ceric ammonium molybdate solution or vanillin/sulfuric acid followed by heating were used as developing agents.

Flash chromatography was performed on E Merck silica gel Si 60 (40–63 mm, Ref 9385). The solvents used were not distilled except petroleum ether and ethyl acetate. Basic silica gel refers to $NaHCO_3$ treated silica gel E Merck Ref 9385.

- *Solvent distillation*

Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone and dichloromethane (CH_2Cl_2) from calcium hydride.

- *Usual procedures*

All air- and/or water-sensitive reactions were carried out under a nitrogen or argon atmosphere with dry, freshly distilled solvents using standard syringe-cannula/septa techniques. All corresponding glassware was oven-dried (110 °C) and/or carefully dried in line with a flameless heat gun. Yields refer to chromatographically and spectroscopically homogeneous materials, unless otherwise stated. Aldehydes **10a–f** and **10h** are commercially available, aldehyde **10g** was prepared as described [26].

- *(E)-3-Methylpent-2-en-4-ynal* **10c**

To a solution of 500 mg (5.2 mmol) of commercial (*E*)-3-methylpent-2-en-4-yn-1-ol in 50 mL of CH_2Cl_2 was added MnO_2 (4.5 g, 52 mmol, 10 equiv). The resulting mixture was stirred at 20 °C for 24 h, filtered on celite, rinsing with CH_2Cl_2, and concentrated in vacuo to give 380 mg (78%) of **10c** which was used directly without purification.

^{1}H NMR (200 MHz, $CDCl_3$) δ 8.62 (d, J = 8.1 Hz, 1H, CHO), 6.08 (dq, J = 8.1, 0.7 Hz, 1H, H-2), 3.55 (s, 1H, H-5), 1.99 (d, J = 0.7 Hz, 3H, CH_3-3).

^{13}C NMR (50 MHz, $CDCl_3$) δ 192.1 (CHO), 140.7 (C-3), 136.5 (C-2), 88.1 (C-5), 79.9 (C-4), 24.4 (CH_3-3).

- *Cyclohex-1-ene-1-carboxaldehyde* **10d**

To a solution of 5 g (47 mmol) of commercial cyclohex-1-ene-1-carbonitrile in 250 mL of diethyl ether at −78 °C was added 47 mL (70 mmol, 1.5 equiv) of an 1.5 M solution of DIBAL-H in toluene. The resulting solution was stirred at −78 °C for 2 h and quenched at −78 °C by addition of 5 mL of saturated aqueous Na_2SO_4 solution. The mixture was allowed to warm to 20 °C and stirred at this temperature for 1 h. $MgSO_4$ was then added and stirring was continued for 1 h. The resulting solution was filtered over celite and concentrated in vacuo (without warming the bath). Purification by flash chromatography (diethyl ether/petroleum ether 10:90 to 50:50) gave 5 g (78%) of aldehyde **10d** as a colorless liquid.

IR (thin film) ν cm^{-1} 2 934, 2 861, 2 820, 2 708, 1 684, 1 642, 1 435, 1 178, 926.

^{1}H NMR (200 MHz, $CDCl_3$) δ 9.36 (s, 1H, CHO), 6.80–6.74 (m, 1H, H-2), 2.34–2.24 (m, 4H, H_2-3, H_2-6), 2.19–2.14 (m, 2H, H_2-4), 1.65–1.50 (m, 4H, H_2-5).

^{13}C NMR (50 MHz, $CDCl_3$) δ 194.1 (CHO), 151.1 (C-2), 141.5 (C-1), 26.4 (C-3), 22.0, 21.2, 21.2 (C-4, C-5, C-6).

MS (GC/MS, EI) m/z 110 (M^+), 95, 81, 67, 53, 39.

• *1-{[(2-Methoxyethoxy)methoxy](tributylstannyl)-methyl}cyclohexene* **9**

To a solution of 10 mL (20 mmol, 1.1 equiv) of hexabutyldistannane in 18 mL of dry THF at −20 °C under Ar was added 13.4 mL (20 mmol, 1.1 equiv) of 1.5 M *n*-BuLi in hexanes. After 30 min, the light green-yellow solution was cooled to −78 °C, and a solution of 2 g (18.2 mmol) of cyclohex-1-ene-1-carboxaldehyde **10d** in 2 mL of THF was added dropwise. After 30 min, the reaction was quenched at −78 °C by addition of a saturated aqueous NH_4Cl solution. The mixture was allowed to warm to 20 °C then extracted with diethyl ether. The combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo to afford 1-[hydroxy(tributylstannyl)methyl]cyclohexene, which was used without further purification.

This material was dissolved in 32 mL of CH_2Cl_2 and cooled to 0 °C under Ar. To this solution was added 9.5 mL (55 mmol, 3 equiv) of *i*-Pr_2NEt followed by 3.3 mL (27 mmol, 1.5 equiv) of (2-methoxyethoxy)methyl chloride (MEMCl) and a few crystals of DMAP. The solution was stirred at 20 °C for 12 h. The reaction mixture was cooled to 0 °C and quenched by addition of a saturated aqueous NH_4Cl solution. The mixture was extracted with diethyl ether and the combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography on silica gel (petroleum ether/diethyl ether 10:90 to 20:80) gave 6.0 g (67%) of α-alkoxy allylic stannane **9** as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (br s, 1H, H-2), 4.62 (d, J = 6.5 Hz, 1H, OC*H*O), 4.53 (d, J = 6.5 Hz, JH-^{117}Sn = JH-^{119}Sn = 5.0 Hz, 1H, OC*H*O), 4.45 (br s, JH-^{117}Sn = JH-^{119}Sn = 33.0 Hz, 1H, H-1′), 3.74–3.50 (m, 3H, OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 2.0–1.70 (m, 4H, 2 CH_2), 1.66–1.37 (m, 4H, 2 CH_2), 1.47 (tt, J = 7.9, 7.3 Hz, 6H, 3 CH_2, $Sn(CH_2CH_2CH_2CH_3)_3$), 1.27 (sex, J = 7.3 Hz, 6H, 3 CH_2, $Sn(CH_2CH_2CH_2CH_3)_3$), 0.86 (t, J = 7.9 Hz, 6H, 3 CH_2, $Sn(CH_2CH_2CH_2CH_3)_3$), 0.86 (t, J = 7.3 Hz, 9H, 3 CH_3, $Sn(CH_2CH_2CH_2CH_3)_3$).

^{13}C NMR (50 MHz, $CDCl_3$) δ 138.1 (C-1), 118.1 (C-2, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 38.0 Hz), 94.0 (OCH_2O, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 37.0 Hz), 76.3 (C-1′), 71.9, 66.9 (OCH_2CH_2O), 58.9 (OCH_3), 29.1 (3 CH_2, $Sn(CH_2CH_2CH_2CH_3)_3$, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 19.0 Hz), 27.5 (3 CH_2, $Sn(CH_2CH_2CH_2CH_3)_3$, J ^{13}C-^{117}Sn = J ^{13}C-^{119}Sn = 54.0 Hz), 26.5, 25.0, 23.0, 22.9 (C-3, C-4, C-5, C-6), 13.6 (3 CH_3, $Sn(CH_2CH_2CH_2CH_3)_3$), 9.6 (3 CH_2, $Sn(CH_2CH_2CH_2CH_3)_3$, J ^{13}C-^{117}Sn = 305.0 Hz, J ^{13}C-^{119}Sn = 292.0 Hz).

MS (CI, NH_3) m/z 491 (MH^+), 308, 218, 201 for Sn^{120} (major isotope, 32%).

Anal calc for $C_{23}H_{46}O_3Sn$: C, 56.46; H, 9.48. Found: C, 56.41; H, 9.64.

• *Typical procedure A: $BF_3{\cdot}OEt_2$-promoted addition of stannane* **9** *to aldehydes* **10a–h**

To a solution of aldehyde **10a–h** (1–5 equiv) in 2 mL of CH_2Cl_2 at −78 °C was added $BF_3{\cdot}OEt_2$ (1–1.5 equiv). After 10 min, a solution of 500 mg (1 mmol, 1 equiv) of the α-alkoxystannane **9** in 2 mL of CH_2Cl_2 was added dropwise at −78 °C. The reaction mixture was stirred for 2–5 h at −78 °C and quenched at −78 °C by addition of a saturated aqueous $NaHCO_3$ solution. The resulting mixture was allowed to warm at 20 °C and extracted with diethyl ether. The combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was then purified by flash chromatography on silica gel.

• *Typical procedure B: $MgBr_2{\cdot}OEt_2$-promoted addition of stannane* **9** *to α- or β-alkoxyaldehyde* **10g,h**

To a solution of $MgBr_2{\cdot}OEt_2$ (795 mg, 3 mmol, 3 equiv) in 2 mL of CH_2Cl_2 at −20 °C was added the hydroxyaldehyde **10g,h** (1.5 equiv). The resulting mixture was then stirred for 45 min at −20 °C. A solution of 500 mg (1 mmol) of the α-alkoxystannane **9** in 2 mL of CH_2Cl_2 was then added and the reaction was allowed to warm to 20 °C. After 24 h the reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution. The mixture was extracted with diethyl ether and the combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was then purified by flash chromatography on silica gel.

• *Typical procedure C: $EtAlCl_2$-promoted addition of stannane* **9** *to aldehydes* **10a,e,f**

To a solution of aldehyde **10a,e,f** (1–5 equiv) in 2 mL of CH_2Cl_2 at −78 °C was added $EtAlCl_2$ (1–1.5 equiv). After 10 min, a solution of 500 mg (1 mmol, 1 equiv) of the α-alkoxystannane **9** in 2 mL of CH_2Cl_2 was added dropwise at −78 °C. The reaction mixture was stirred for 2–5 h at −78 °C and quenched at −78 °C by addition of a saturated aqueous $NaHCO_3$ solution. The resulting mixture was allowed to warm to 20 °C and extracted with diethyl ether. The combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was then purified by flash chromatography on silica gel.

• *{[(2-Methoxyethoxy)methoxy]methylidene}cyclohexane*

To a solution of α-alkoxystannane **9** (500 mg, 1 mmol) in 2 mL of CH_2Cl_2 at −78 °C was added $BF_3{\cdot}OEt_2$ (1.3 mL, 0.1 mmol, 0.1 equiv). The reaction mixture was stirred for 1 h at −78 °C and quenched at −78 °C by addition of a saturated aqueous $NaHCO_3$ solution. The resulting mixture was allowed to warm to 20 °C and extracted with diethyl ether. The combined extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by flash chromatography on neutralized silica gel gave 190 mg (38%) of starting material **9** and 127 mg (62%) of {[(2-methoxyethoxy)-methoxy]methylidene}cyclohexane corresponding to the hydrolysis product of the postulated intermediate **12**.

IR (thin film) ν cm^{-1} 2 926, 2 852, 1 689, 1 447, 1 214, 1 178, 1 136, 1 104, 1 053, 994, 842.

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (br s, 1H, H-1′), 4.82 (s, 2H, OCH_2O), 3.70–3.67 and 3.54–3.52 (2m, 4H, OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 2.18–2.15 (m, 2H, H_2-2), 1.93–1.91 (m, 2H, H_2-7), 1.47–1.44 (m, 6H, H_2-3, H_2-4, H_2-5).

^{13}C NMR (50 MHz, $CDCl_3$) δ 134.9 (C-1′), 120.7 (C-1), 95.4 (OCH_2O), 71.8, 67.2 (OCH_2CH_2O), 59.0 (OCH_3), 30.7, 28.3, 27.1, 26.9, 25.7 (C-2, C-3, C-4, C-5, C-6).

MS (GC/MS, CI, NH_3) m/z 218 ($MH^+ + NH_3$), 201 (MH^+), 154, 106, 94.

• *Condensation of* **9** *and benzaldehyde* **10a**

$BF_3{\cdot}OEt_2$-promoted condensation of **9** and benzaldehyde **10a** according to procedure A gave in 84% overall yield an 83:0:6:11 mixture of ***syn-E/syn-Z/anti-E/anti-Z* 11a** isomers from which the major ***syn-E* 11a** was purified by silica-gel flash chromatography. Compound ***syn-E* 11a** was also purified by silica-gel flash chromatography from a 63:16:7:14 mixture of the same ***syn-E/syn-Z/anti-E/anti-Z* 11a** isomers obtained in 95% overall yield using $EtAlCl_2$ as described in procedure C. Compounds ***syn-Z* 11a**, ***anti-E* 11a** and ***anti-Z* 11a** were not separated, NMR assignments were deduced from ^{1}H and ^{13}C NMR spectra of various mixtures of isomers with the aid of NOESY experiments when necessary.

■ *[1R*(1S*,2E)]-α-(2-{[(2-Methoxyethoxy)methoxy]-methylidene}cyclohexyl)benzenemethanol* (**syn-E 11a**)

Mp 65 °C (petroleum ether/diethyl ether, 5:1).

IR (KBr) ν cm^{-1} 3 452, 2 915, 2 857, 1 708, 1 686, 1 454, 1 292, 1 239, 1 180, 1 148, 1 098, 1 057, 1 023, 999, 849, 759, 702.

^1H NMR (400 MHz, $CDCl_3$, NOESY experiment) δ 7.23–7.12 (m, 5H, Ar-H), 5.54 (br s, 1H, CH-1″), 4.83 (d, J = 8.7 Hz, 1H, H-1), 4.56 and 4.53 (2d, J = 6.5 Hz, 2H, OCH_2O), 3.44–3.30 (m, 4H, OCH_2CH_2O), 3.28 (s, 3H, CH_3, OCH_3), 2.34 (dt, J = 14.0, 4.2 Hz, 1H, H-3′a), 2.19 (dt, J = 8.7, 4.3 Hz, 1H, H-1′), 2.07–2.04 (m, 2H, H_2-6′), 1.91–1.84 (m, 1H, H-3′b), 1.69–1.59 (m, 2H), 1.51–1.41 (m, 2H), 1.33–1.27 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 144.5 (C, Ar), 137.8 (C-1″), 128.2, 127.5, 126.5 (C, Ar), 119.0 (C-2′), 95.3 (OCH_2O), 73.8 (C-1), 71.8, 67.2 (OCH_2CH_2O), 59.0 (OCH_3), 47.0 (C-1′), 27.9, 27.1, 23.8, 22.9 (C-3′, C-4′, C-5′, C-6′).

MS (GC/MS, CI, NH_3) m/z 324 ($MH^+ + NH_3$), 307 (MH^+), 306, 289, 218, 201.

Anal calc for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55. Found: C, 70.75; H, 8.54.

■ *[1R*(1S*,2Z)]-α-(2-{[(2-Methoxyethoxy)methoxy]-methylidene}cyclohexyl)benzenemethanol* (**syn-Z 11a**), *[1R*(1R*,2E)]-α-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)benzenemethanol* (**anti-E 11a**) *and [1R*(1R*,2Z)]-α-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)benzenemethanol* (**anti-Z 11a**)

IR (KBr) ν cm^{-1} 3 492, 2 927, 2 856, 1 708, 1 681, 1 450, 1 180, 1 128, 1 053, 922, 854, 758, 702.

^1H NMR (400 MHz, $CDCl_3$, mixture of three isomers):

syn-Z 11a, δ 7.30–7.19 (m, 5H, Ar-H), *6.25* (br s, 1H, CH-1″), 4.85 (s, 2H, OCH_2O), 4.67 (d, J = 10.4 Hz, 1H, H-1), 3.75, 3.65, 3.48 (3m, 4H, OCH_2CH_2O), 3.32 (s, 3H, CH_3, OCH_3), *3.03* (dt, J = 10.5, 4.1 Hz, 1H, H-1′), *2.65* (m, H-3′a), 2.65 (m, 1H), 1.85 (m, 1H), 1.70–1.20 (m, 5H).

anti-E 11a, δ 7.23–7.12 (m, 5H, Ar-H), *5.76* (br s, 1H, CH-1″), *4.29* (d, J = 6.5 Hz, 1H, H-1), 4.56 and 4.53 (2d, J = 6.5 Hz, 2H, OCH_2O), 3.44–3.30 (m, 4H, OCH_2CH_2O), 3.28 (s, 3H, CH_3, OCH_3), 2.34 (dt, J = 14.0, 4.2 Hz, 1H, H-3′a), 2.19 (dt, J = 8.7, 4.3 Hz, 1H, H-1′), 2.07–2.04 (m, 2H, H_2-6′), 1.91–1.84 (m, 1H, H-3′b), 1.69–1.59 (m, 2H), 1.51–1.41 (m, 2H), 1.33–1.27 (m, 1H).

anti-Z 11a: δ 7.30–7.19 (m, 5H, Ar-H), *6.18* (br s, 1H, CH-1″), 4.85 (s, 2H, OCH_2O), *4.62* (d, J = 10.2 Hz, 1H, H-1), 3.75, 3.65, 3.48 (3m, 4H, OCH_2CH_2O), 3.31 (s, 3H, CH_3, OCH_3), *2.08* (m, 1H, H-1′), *1.97* (m, 2H, H_2-3′), 1.70–1.20 (m, 5H).

^{13}C NMR (50 MHz, $CDCl_3$, mixture of three isomers, two major isomers assigned):

syn-Z 11a, δ 143.2 (C, Ar), 139.5 (C-1″), 128.3 (C, Ar), 118.90 (C-2′), 95.5 (OCH_2O), 73.3 (C-1), 71.7 (OCH_2CH_2O), 67.6 (OCH_2CH_2O), 59.0 (OCH_3), 42.5 (C-1′), 28.0, 27.6, 27.1, 22.1 (C-3′, C-4′, C-5′, C-6′).

anti-Z 11a, δ 142.8 (C, Ar), 138.7 (C-1″), 127.6, 127.2 (C, Ar), 118.90 (C-2′), 95.2 (OCH_2O), 72.1 (C-1), 71.7, 67.3 (OCH_2CH_2O), 59.0 (OCH_3), 47.6 (C-1′), 28.6, 28.0, 26.8, 22.3 (C-3′, C-4′, C-5′, C-6′).

MS (GC/MS, CI, NH_3) m/z 324 ($MH^+ + NH_3$), 307 (MH^+), 306, 289, 218, 201.

• *Condensation of* **9** *and crotonaldehyde* **10b**

Compound **syn-E 11b** was purified by chromatography on silicagel from an 85:9:3:3 mixture of **syn-E/syn-Z/anti-E/anti-Z 11b** isomers obtained in overall 80% yield using $BF_3{\cdot}OEt_2$ as described in procedure A. Compounds **syn-Z 11b/anti-E 11b/anti-Z 11b** were not separated and NMR respective assignments were made as above.

■ *[1R*(1R*,2E)]-1-(2-{[(2-Methoxyethoxy)methoxy]-methylidene}cyclohexyl)but-2-en-1-ol* (**syn-E 11b**)

IR (thin film) ν cm^{-1} 3 447, 2 924, 2 855, 1 682, 1 448, 1 179, 1 132, 1 099, 1 052, 1 028, 975, 850.

^1H NMR (400 MHz, $CDCl_3$, NOESY experiment) δ 6.00 (br s, 1H, H-1″), 5.60 (dq, J = 15.2, 6.4 Hz, 1H, H-3), 5.42 (dd, J = 15.2, 7.6 Hz, 1H, H-2), 4.82 (br s, 2H, OCH_2O), 4.22 (t, J = 7.6 Hz, 1H, H-1), 3.71–3.61 and 3.53–3.50 (2m, 4H, OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 2.38 (dt, J = 13.7, 4.1 Hz, 1H, H-3′a), 1.99–1.94 (m, 1H, H-1′), 1.93–1.76 (m, 2H), 1.64 (d, J = 6.4 Hz, 3H, CH_3, CH_3-3), 1.61–1.55 (m, 2H), 1.53–1.45 (m, 2H), 1.37–1.28 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 137.1 (C-1″), 133.8 (C-3), 126.5 (C-2), 120.0 (C-2′), 95.3 (OCH_2O), 71.7 (C-1), 71.7, 67.1 (OCH_2CH_2O), 59.0 (OCH_3), 45.4 (C-1′), 28.0, 27.0, 23.6, 22.7 (C-3′, C-4′, C-5′, C-6′), 17.7 (CH_3-3).

MS (GC/MS, EI) m/z 270 (M^+), 199, 111, 89, 59.

Anal calc for $C_{15}H_{26}O_4$: C, 66.63; H, 9.69. Found: C, 66.72; H, 9.83.

■ *[1R*(1R*,2Z)]-1-(2-{[(2-Methoxyethoxy)methoxy]-methylidene}cyclohexyl)but-2-en-1-ol* (**syn-Z 11b**), *[1R*(1S*,2E)]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)but-2-en-1-ol* (**anti-E 11b**) *and [1R*(1S*,2Z)]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)but-2-en-1-ol* (**anti-Z 11b**)

IR (thin film), ν cm^{-1} 3 447, 2 924, 2 855, 1 682, 1 448, 1 179, 1 132, 1 099, 1 052, 1 028, 975, 850.

^1H NMR (400 MHz, $CDCl_3$, mixture of three isomers):

syn-Z 11b, δ *6.09* (br s, 1H, H-1″), 5.60 (dq, J = 15.2, 6.4 Hz, 1 H, H-3), 5.42 (dd, J = 15.2, 7.6 Hz, 1H, H-2), 4.82 (br s, 2H, OCH_2O), 4.22 (t, J = 7.6 Hz, 1H, H-1), 3.71–3.61 and 3.53–3.50 (2m, 4H, OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 2.38 (dt, J = 13.7, 4.1 Hz, 1 H, H-3′a), 1.99–1.94 (m, 1H, H-1′), 1.93–1.76 (m, 2H), 1.64 (d, J = 6.4 Hz, 3H, CH_3, CH_3-3), 1.61–1.55 (m, 2H), 1.53–1.45 (m, 2H), 1.37–1.28 (m, 1H).

anti-E 11b: δ 6.05 (br s, 1H, H-1″), 5.60 (dq, J = 15.2, 6.4 Hz, 1H, H-3), 5.42 (dd, J = 15.2, 7.6 Hz, 1H, H-2), 4.82 (br s, 2H, OCH_2O), 4.22 (t, J = 7.6 Hz, 1H, H-1), 3.71–3.61 and 3.53–3.50 (2m, 4H, OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 2.38 (dt, J = 13.7, 4.1 Hz, 1H, H-3′a), 1.99–1.94 (m, 1H, H-1′), 1.93–1.76 (m, 2H), 1.64 (d, J = 6.4 Hz, 3H, CH_3, CH_3-3), 1.61–1.55 (m, 2H), 1.53–1.45 (m, 2H), 1.37–1.28 (m, 1H).

anti-Z 11b, δ 6.02 (br s, 1H, H-1″), 5.60 (dq, J = 15.2, 6.4 Hz, 1H, H-3), 5.42 (dd, J = 15.2, 7.6 Hz, 1H, H-2), 4.82 (br s, 2H, OCH_2O), 4.22 (t, J = 7.6 Hz, 1H, H-1), 3.71–3.61 and 3.53–3.50 (2m, 4H, OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 2.38 (dt, J = 13.7, 4.1 Hz, 1H, H-3′a), 1.99–1.94 (m, 1H, H-1′), 1.93–1.76 (m, 2H), 1.64 (d, J = 6.4 Hz, 3H, CH_3, CH_3-3), 1.61–1.55 (m, 2H), 1.53–1.45 (m, 2H), 1.37–1.28 (m, 1H).

MS (GC/MS, EI) m/z 270 (M^+), 199, 111, 89, 59.

• *Condensation of* **9** *and (E) 3-methylpent-2-en-4-ynal* **10c**

Compounds **syn-E 11c**, and **syn-Z 11c/anti-E 11c/anti-Z 11c** isomers were obtained as a 90:10 mixture in 63% yield using $BF_3{\cdot}OEt_2$ as described in procedure A and were not separated. NMR assignments of each isomer were made as above.

■ *[1R*(1R*,2E),2Z]-1-(2-{[(2-Methoxyethoxy)-methoxy]methylidene}cyclohexyl)-3-methylpent-2-en-4-yn-1-ol* ***(syn-E 11c)***,
[1R(1R*,2Z),2Z]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)-3-methylpent-2-en-4-yn-1-ol* ***(syn-Z 11c)***,
[1R(1S*,2E),2Z]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)-3-methylpent-2-en-4-yn-1-ol* ***(anti-E 11c)*** *and*
[1R(1S*,2Z),2Z]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)-3-methylpent-2-en-4-yn-1-ol* ***(anti-Z 11c)***

IR (thin film) ν cm^{-1} 3 418, 2 925, 1 636, 1 449, 1 009, 901, 851.

^1H NMR (400 MHz, $CDCl_3$, mixture of four isomers):

***syn-E* 11c**, δ *5.94* (br s, 1H, H-1″), 5.62 (d, J = 8.6 Hz, 1H, H-2), 4.81 (br s, 2H, OCH_2O), 4.75 (t, J = 8.6 Hz, 1H, H-1), 3.68–3.62 and 3.52–3.49 (2m, 4H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 3.09 (s, 1H, H-5), 2.41 (dt, J = 14.0, 4.1 Hz, 1H, H-3′a), 2.03–1.92 (m, 2H), 1.90–1.80 (m, 1H, H-6a), 1.82 (s, 3H, CH_3, CH_3-3), 1.65–1.57 (m, 2H), 1.53–1.45 (m, 2H), 1.31–1.20 (m, 1H).

***syn-Z* 11c**, δ *6.08* (br s, 1H, H-1″), 5.62 (d, J = 8.6 Hz, 1H, H-2), 4.81 (br s, 2H, OCH_2O), 4.75 (t, J = 8.6 Hz, 1H, H-1), 3.68–3.62 and 3.52–3.49 (2m, 4H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 3.09 (s, 1H, H-5), 2.41 (dt, J = 14.0, 4.1 Hz, 1H, H-3′a), 2.03–1.92 (m, 2H), 1.90–1.80 (m, 1H, H-6a), 1.82 (s, 3H, CH_3, CH_3-3), 1.65–1.57 (m, 2H), 1.53–1.45 (m, 2H), 1.31–1.20 (m, 1H).

***anti-E* 11c**, δ *5.99* (br s, 1H, H-1″), 5.62 (d, J = 8.6 Hz, 1H, H-2), 4.81 (br s, 2H, OCH_2O), 4.75 (t, J = 8.6 Hz, 1H, H-1), 3.68–3.62 and 3.52–3.49 (2m, 4H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 3.09 (s, 1H, H-5), 2.41 (dt, J = 14.0, 4.1 Hz, 1H, H-3′a), 2.03–1.92 (m, 2H), 1.90–1.80 (m, 1H, H-6a), 1.82 (s, 3H, CH_3, CH_3-3), 1.65–1.57 (m, 2H), 1.53–1.45 (m, 2H), 1.31–1.20 (m, 1H).

***anti-Z* 11c**, δ *6.00* (br s, 1H, H-1″), 5.62 (d, J = 8.6 Hz, 1H, H-2), 4.81 (br s, 2H, OCH_2O), 4.75 (t, J = 8.6 Hz, 1H, H-1), 3.68–3.62 and 3.52–3.49 (2m, 4H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 3.09 (s, 1H, H-5), 2.41 (dt, J = 14.0, 4.1 Hz, 1H, H-3′a), 2.03–1.92 (m, 2H), 1.90–1.80 (m, 1H, H-6a), 1.82 (s, 3H, CH_3, CH_3-3), 1.65–1.57 (m, 2H), 1.53–1.45 (m, 2H), 1.31–1.20 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$ mixture of isomers, one isomer assigned):

***syn-E* 11c**, δ 141.4 (C-2), 137.3 (C-1″), 120.2 (C-2′), 119.2 (C-3), 95.5 (OCH_2O), 82.6 (C-4), 81.6 (C-5), 71.9, 67.4 (OCH_2CH_2O), 69.6 (C-1), 59.0 (OCH_3), 45.3 (C-1′), 28.0, 27.1, 23.8, 22.9 (C-3′, C-4′, C-5′, C-6′), 23.0 (CH_3-3).

MS (GC/MS, EI) m/z 294 (M^+), 265, 199, 95, 89, 59.

• *Condensation of* ***9*** *and cyclohex-1-ene-1-carboxaldehyde* ***10d***

Using $BF_3{\cdot}OEt_2$ as described in procedure A afforded after flash chromatography the homoallylic alcohol ***syn-E* 11d** and the dihydroxy derivative **13** in 69 and 17% respective yields.

■ *[1R*(1S*,2E)]-α-Cyclohex-1-enyl-2-{[(2-methoxyethoxy)methoxy]methylidene}cyclohexanemethanol* ***(syn-E 11d)***

IR (thin film) ν cm^{-1} 3 455, 2 924, 2 855, 1 682, 1 447, 1 179, 1 136, 1 099, 1 051, 1 027, 993, 910, 850.

^1H NMR (400 MHz, $CDCl_3$) δ 6.00 (br s, 1H, H-1″), 5.59 (br s, 1H, H-2′), 4.82 (br s, 2H, OCH_2O), 4.21 (d, J = 9.4 Hz, 1H, H-1), 3.70–3.66 and 3.55–3.52 (2m, 4H, OCH_2CH_2O), 3.38 (s, 3H, CH_3, OCH_3), 2.41 (dt, J = 13.8, 4.1 Hz, 1H, H-3″a), 2.18–2.14 (m, 1H, H-1″), 2.00–1.80 (m, 7H), 1.72–1.45 (m, 7H), 1.36–1.24 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 139.3 (C-1′), 136.5 (C-1″), 123.7 (C-2′), 120.3 (C-2″), 95.2 (OCH_2O), 75.3 (C-1), 71.6, 67.1 (OCH_2CH_2O), 58.9 (OCH_3), 42.4 (C-1″), 28.0, 27.1, 25.0, 23.1, 23.1, 22.6, 22.6, 22.3 (C-3′, C-4′, C-5′, C-6′, C-3″, C-4″, C-5″, C-6″).

MS (GC/MS, CI, NH_3) m/z 328 (MH^+ + NH_3), 310 (MH^+ + NH_3 − H_2O), 293, 217, 199.

Anal calc for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.51; H, 9.57.

■ *(1R*,2S*)-1,2-Di(cyclohex-1-enyl)-2-[(2-methoxyethoxy)methoxy]ethanol* ***13***

IR (thin film) ν cm^{-1} 3 475, 2 926, 2 855, 1 667, 1 447, 1 136, 1 107, 1 021, 976, 921, 841.

^1H NMR (400 MHz, $CDCl_3$) δ 5.65 (br s, 1H, H-2′), 5.63 (br s, 1H, H-2″), 4.69, 4.61 (2d, 2H, J = 6.8 Hz, OCH_2O), 3.98 (d, 1H, J = 8.4 Hz, H-1), 3.90 (d, 1H, J = 8.4 Hz, H-2), 3.84–3.78, 3.66–3.61 and 3.56–3.50 (3m, 1H, 1H and 2H respectively, OCH_2CH_2O), 3.67 (s, 3H, CH_3, OCH_3), 2.94 (br s, OH), 2.07–1.70 (m, 8H), 1.60–1.40 (m, 8H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 136.3, 134.1 (C-1′, C-1″), 127.9, 125.8 (C-2′, C-2″), 93.0 (OCH_2O), 84.0 (C-2), 77.5 (C-1), 72.0, 67.6 (OCH_2CH_2O), 59.0 (OCH_3), 25.2 (3 CH_2), 24.0 (CH_2), 22.6 (4 CH_2).

MS (GC/MS, CI, NH_3): 328 (MH^+ + NH_3), 310 (MH^+ + NH_3 − H_2O), 293, 222, 205, 187, 94.

• *Condensation of* ***9*** *and 2-methylpropanal* ***10e***

The ***syn-E/syn-Z/anti-E/anti-Z* 11e** isomers were obtained as a 73:2:23:2 mixture in 69% overall yield using $EtAlCl_2$ as described in procedure C and were not separated. NMR assignments of each isomer were deduced from ^1H, ^{13}C NMR spectra and NOESY experiments. Procedure A using $BF_3{\cdot}OEt_2$ gave only 13% yield of a complex mixture of the same four isomers.

■ *[1R*(1R*,2E)]-1-(2-{[(2-Methoxyethoxy)methoxy]-methylidene}cyclohexyl)-2-methylpropan-1-ol* ***(syn-E 11e)***,
[1R(1R*,2Z)]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)-2-methylpropan-1-ol* ***(syn-Z 11e)***,
[1R(1S*,2E)]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)-2-methylpropan-1-ol* ***(anti-E 11e)*** *and*
[1R(1S*,2Z)]-1-(2-{[(2-methoxyethoxy)methoxy]-methylidene}cyclohexyl)-2-methylpropan-1-ol* ***(anti-Z 11e)***

IR (thin film) ν cm^{-1} 3 485, 2 927, 1 682, 1 449, 1 366, 1 256, 1 215, 1 179, 1 130, 1 051, 993, 848.

^1H NMR (400 MHz, $CDCl_3$, mixture of four isomers):

***syn-E* 11e**, δ *6.02* (br s, 1H, H-1″), *4.82* (br s, 2H, OCH_2O), 3.68–3.64 (m, 3H, H-1 and OCH_2CH_2O), 3.54–3.50 (m, 2H, OCH_2CH_2O), 3.34 (s, 3H, CH_3, OCH_3), *2.44* (dt, J = 13.5, 4.1 Hz, 1H, H-3′a), 2.07–2.03 (m, 1H, H-1′), 1.97–1.92 (m, 1H), 1.89–1.20 (m, 6H), 0.91 (d, J = 7.0 Hz, 3H, CH_3, CH_3-2), 0.78 (d, J = 7.0 Hz, 3H, H_3-3).

***syn-Z* 11e**, δ *6.18* (br s, 1H, H-1″), 4.81 (s, 2H, OCH_2O), 3.68–3.64 and (m, 3H, H-1 and OCH_2CH_2O), 3.54–3.50 (m, 2H, OCH_2CH_2O), 3.34 (s, 3H, CH_3, OCH_3), 2.60 (dt, J = 13.7, 4.1 Hz, 1H, H-3′a), 2.07–2.03 (m, 1H, H-1′), 1.97–1.20 (m, 7H), 1.02 (d, J = 6.9 Hz, 3H, CH_3, CH_3-2), 0.78 (d, J = 7.0 Hz, 3H, H_3-3).

***anti-E* 11e**, δ 6.06 (br s, 1H, H-1″), 4.81 (s, 2H, OCH_2O), 3.68–3.64 (m, 3H, H-1 and OCH_2CH_2O), 3.54–3.50 (m, 2H, OCH_2CH_2O), 3.34 (s, 3H, CH_3, OCH_3), *2.60* (dt, J = 13.7, 4.1 Hz, 1H, H-3′a), 2.07–2.03 (m, 1H,

H-1′), 1.97–1.20 (m, 7H), 1.02 (d, J = 6.9 Hz, 3H, CH_3, CH_3-2), 0.78 (d, J = 7.0 Hz, 3H, H_3-3).

***anti-Z* 11e**, *δ 6.00* (br s, 1H, H-1″), 4.83 (s, 2H, OCH_2O), 3.68–3.64 (m, 3H, H-1 and OCH_2CH_2O), 3.54–3.50 (m, 2H, OCH_2CH_2O), 3.34 (s, 3H, CH_3, OCH_3), 2.60 (dt, J = 13.7, 4.1 Hz, 1H, H-3′a), 2.07–2.03 (m, 1H, H-1′), 1.97–1.20 (m, 7H), 1.02 (d, J = 6.9 Hz, 3H, CH_3, CH_3-2), 0.78 (d, J = 7.0 Hz, 3H, H_3-3).

^{13}C NMR (100 MHz, $CDCl_3$ mixture of isomers, two isomers assigned):

***syn-E* 11e**, *δ* 136.4 (C-1″), 121.0 (C-2′), 95.3 (OCH_2O), 74.0 (C-1), 71.7, 67.2 (OCH_2CH_2O), 59.0 (OCH_3), 42.4 (C-1′), 29.5 (C-2), 28.2, 27.4, 23.3, 22.4 (C-3′, C-4′ C-5′, C-6′), 20.8 (CH_3-2), 14.3 (C-3).

***anti-E* 11e**, *δ* 137.9 (C-1″), 119.9 (C-2′), 95.3 (OCH_2O), 71.9 (C-1), 71.7, 67.2 (OCH_2CH_2O), 59.0 (OCH_3), 42.8 (C-1′), 28.9 (C-2), 28.8, 27.0, 23.3, 22.5 (C-3′, C-4′ C-5′, C-6′), 21.1 (CH_3-2), 13.7 (C-3).

MS (GC/MS, CI, NH_3) m/z 290 ($MH^+ + NH_3$), 273 (MH^+), 184, 167.

Anal calc for $C_{15}H_{28}O_4$: C, 66.14; H, 10.36. Found: C, 65.79; H, 10.35.

• *Condensation of* ***9*** *and cyclohexane-1-carboxaldehyde* ***10f***

The ***syn-E/syn-Z/anti-E/anti-Z* 11f** isomers were obtained as an 82:3:12:3 mixture in 61% yield using $EtAlCl_2$ as described in procedure C and were not separated. NMR assignments of each isomer were deduced from ^1H and ^{13}C NMR spectra as well as NOESY experiments carried out on different mixtures of the four isomers. Procedure A using $BF_3{\cdot}OEt_2$ did not gave any homoaldol product.

■ *[1R* (1R*,2E)]-α-Cyclohexyl-2{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexanemethanol* ***(syn-E 11f)***, *[1R* (1R*,2Z)]-α-cyclohexyl-2{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexanemethanol* ***(syn-Z 11f)***, *[1R* (1S*,2E)]-α-cyclohexyl-2{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexanemethanol* ***(anti-E 11f)*** *and [1R* (1S*,2Z)]-α-cyclohexyl-2{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexanemethanol* ***(anti-Z 11f)***

IR (thin film) ν cm^{-1} 3 482, 2 924, 2 851, 1 682, 1 448, 1 366, 1 256, 1 215, 1 179, 1 129, 1 098, 1 050, 1 028, 990, 848.

^1H NMR (400 MHz, $CDCl_3$, mixture of four isomers):

***syn-E* 11f**, *δ 6.04* (br s, 1H, H-1‴), 4.84 (br s, 2H, OCH_2O), 3.74–3.66 and 3.57–3.52 (2m, 4H, OCH_2CH_2O), 3.66–3.63 (m, 1H, H-1), 3.37 (s, 3H, CH_3, OCH_3), 2.42 (dt, J = 13.4, 4.1 Hz, 1H, H-3″a), 2.14–2.11 (m, 1H, H-1″), 1.99–1.93 (m, 18H).

***syn-Z* 11f**, *δ 6.18* (br s, 1H, H-1‴), 4.84 (br s, 2H, OCH_2O), 3.74–3.66 and 3.57–3.52 (2m, 4H, OCH_2CH_2O), 3.66–3.63 (m, 1H, H-1), 3.37 (s, 3H, CH_3, OCH_3), 2.42 (dt, J = 13.4, 4.1 Hz, 1H, H-3″a), 2.14–2.11 (m, 1H, H-1″), 1.99–1.93 (m, 18H).

***anti-E* 11f**, *δ 6.06* (br s, 1H, H-1‴), 4.84 (br s, 2H, OCH_2O), 3.74–3.66 and 3.57–3.52 (2m, 4H, OCH_2CH_2O), 3.66–3.63 (m, 1H, H-1), 3.37 (s, 3H, CH_3, OCH_3), 2.60 (dt, J = 13.4, 4.1 Hz, 1H, H-3″a), 2.14–2.11 (m, 1H, H-1″), 1.99–1.93 (m, 18H).

***anti-Z* 11f**, *δ 6.01* (br s, 1H, H-1‴), 4.84 (br s, 2H, OCH_2O), 3.74–3.66 and 3.57–3.52 (m, 2H, OCH_2CH_2O), 3.66–3.63 (m, 1H, H-1), 3.37 (s, 3H, CH_3, OCH_3), 2.42 (dt, J = 13.4, 4.1 Hz, 1H, Ha-3″), 2.14–2.11 (m, 1H, H-1″), 1.99–1.93 (m, 18H).

^{13}C NMR (50 MHz, $CDCl_3$, the major isomer out of the four was assigned):

***syn-E* 11f**, *δ* 136.2 (C-1‴), 120.7 (C-2″), 95.0 (OCH_2O), 73.4 (C-1), 71.5, 67.0 (OCH_2CH_2O), 58.9 (OCH_3), 41.4 (C-1″), 39.5 (C-1′), 31.0, 28.5, 28.0, 26.9, 26.9, 26.5, 24.8, 23.1, 22.0 (C-3, C-4, C-5, C-6, C-7, C-3′, C-4′, C-5′, C-6′).

MS (ID, CI, NH_3) m/z 330 ($MH^+ + NH_3$), 313 (MH^+), 224, 207, 189.

Anal calc for $C_{18}H_{32}O_4$: C, 69.19; H, 10.33. Found: C, 69.31; H, 10.29.

• *Condensation of* ***9*** *and 3-(benzyloxy)propanal* ***10g***

The ***syn-E/syn-Z/anti-E/anti-Z* 11g** isomers were obtained as an 80:6:8:6 mixture in 70% overall yield using $BF_3{\cdot}OEt_2$ as described in procedure A, and were not separated. NMR signals of each isomer were assigned as above with the aid of careful NOESY experiments. In presence of $MgBr_2{\cdot}OEt_2$ at −78 °C, according to procedure B, homoallylic alcohols ***syn-E* 11g** and ***anti-E* 11g** were also obtained as a 4:96 mixture in 64% yield together with 33% starting material.

■ *[1R* (1R*,2E)]-3-Benzyloxy-1-(2-{[(2-methoxyethoxy]methoxy]methylidene}cyclohexyl)propan-1-ol* ***(syn-E 11g)***, *[1R* (1R*,2Z)]-3-benzyloxy-1-(2-{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexyl)propan-1-ol* ***(syn-Z 11g)***, *[1R* (1S*,2E)]-3-benzyloxy-1-(2-{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexyl)propan-1-ol* ***(anti-E 11g)*** *and [1R* (1S*,2Z)]-3-benzyloxy-1-(2-{[(2-methoxyethoxy)-methoxy]methylidene}cyclohexyl)propan-1-ol* ***(anti-Z 11g)***

IR (thin film) ν cm^{-1} 3 490, 2 924, 1 681, 1 453, 1 365, 1 179, 1 099, 1 051, 1 028, 990.

^1H NMR (400 MHz, $CDCl_3$, four isomers):

***syn-E* 11g**, *δ* 7.34–7.26 (m, 5H, Ar-H), *5.99* (br s, 1H, H-1″), 4.83 (br s, 2H, OCH_2O), 4.49 (br s, 2H, $ArCH_2O$), 4.01 (t, J = 9.1 Hz, 1H, H-1), 3.74–3.60 (m, 4H, H_2-3 and OCH_2CH_2O), 3.53–3.50 (m, 2H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 2.49 (dt, J = 13.8, 4.2 Hz, 1H, H-3′a), 2.11–2.07 (m, 1H, H-3′b), 1.95–1.91 (m, 1H, H-1′), 1.85–1.78 (m, 1H), 1.74–1.65 (m, 2H), 1.65–1.45 (m, 3H), 1.45–1.35 (m, 1H), 1.32–1.22 (m, 1H).

***syn-Z* 11g**, *δ* 7.32–7.23 (m, 5H, Ar-H), *6.20* (br s, 1H, H-1″), 4.85 (br s, 2H, OCH_2O), 4.51 (br s, 2H, $ArCH_2O$), 3.89 (t wide, J = 9.0 Hz, 1H, H-1), 3.78–3.65 (m, 4H, H_2-3 and OCH_2CH_2O), 3.55–3.50 (m, 2H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 2.57 (dt, J = 13.9, 3.9 Hz, 1H, H-3′a), 2.23 (br s, 1H, OH), 2.01–1.81 (m, 3H), 1.77–1.50 (m, 3H), 1.50–1.45 (m, 3H), 1.35–1.20 (m, 1H).

***anti-E* 11g**, *δ* 7.32–7.23 (m, 5H, Ar-H), *6.05* (br s, 1H, H-1″), 4.85 (br s, 2H, OCH_2O), 4.51 (br s, 2H, $ArCH_2O$), 3.89 (t wide, J = 9.0 Hz, 1H, H-1), 3.78–3.65 (m, 4H, H_2-3 and OCH_2CH_2O), 3.55–3.50 (m, 2H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 2.57 (dt, J = 13.9, 3.9 Hz, 1H, H-3′a), 2.23 (br s, 1H, OH), 2.01–1.81 (m, 3H), 1.77–1.50 (m, 3H), 1.50–1.45 (m, 3H), 1.35–1.20 (m, 1H).

***anti-Z* 11g**, *δ* 7.32–7.23 (m, 5H, Ar-H), *6.02* (br s, 1H, H-1″), 4.85 (br s, 2H, OCH_2O), 4.51 (br s, 2H, $ArCH_2O$), 3.89 (t wide, J = 9.0 Hz, 1H, H-1), 3.78–3.65 (m, 4H, H_2-3 and OCH_2CH_2O), 3.55–3.50 (m, 2H, OCH_2CH_2O), 3.35 (s, 3H, CH_3, OCH_3), 2.57 (dt, J = 13.9, 3.9 Hz, 1H, H-3′a), 2.23 (br s, 1H, OH), 2.01–1.81 (m, 3H), 1.77–1.50 (m, 3H), 1.50–1.45 (m, 3H), 1.35–1.20 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$, mixture of four isomers, two isomers assigned):

***syn-E* 11g**, *δ* 138.4 (C, Ar), 137.1 (C-1″), 128.5, 128.4, 128.8 (C, Ar), 121.0 (C-2′), 95.5 (OCH_2O), 73.5

($ArCH_2O$), 71.9, 67.5 (OCH_2CH_2O), 69.7, 69.7 (C-1, C-3), 59.0 (OCH_3), 45.9 (C-1′), 35.1 (C-2), 28.1, 27.3, 23.4, 22.6 (C-3′, C-4′, C-5′, C-6′).

***anti-E* 11g**, δ 138.6 (C, Ar), 138.1 (C-1″), 128.4, 127.7, 127.6 (C, Ar), 119.7 (C-2′), 95.5 (OCH_2O), 73.3 ($ArCH_2O$), 71.9, 76.4 (OCH_2CH_2O), 68.4 (C-3), 67.7 (C-1), 59.0 (OCH_3), 46.0 (C-1′), 34.6 (C-2), 29.3, 27.0, 22.6, 22.6 (C-3′, C-4′, C-5′, C-6′).

MS (GC/MS, CI, NH_3) m/z 382 ($MH^+ + NH_3$), 365 (MH^+), 347, 289, 276, 259, 182.

Anal calc for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 68.96; H, 8.58.

• *Condensation of* ***9*** *and 2-(benzyloxy)acetaldehyde* ***10h***

The ***syn-E/syn-Z/anti-E/anti-Z* 11h** isomers were obtained as a 72:14:12:2 mixture in 46% overall yield using $BF_3{\cdot}OEt_2$ as described in procedure A, and were not separated. NMR assignments were made as above. Compounds ***syn-E* 11h/*anti-E* 11h** were also obtained as a 10:90 mixture in 78% yield using $MgBr_2{\cdot}OEt_2$ as described in procedure B (−20 to 20 °C).

■ *[1R*(1S*,2E)]-2-Benzyloxy-1-(2-{[(2-methoxyethoxy)methoxy]methylidene}cyclohexyl)ethanol* ***(syn-E* 11h)**, *[1R*(1S*,2E)]-2-benzyloxy-1-(2-{[(2-methoxyethoxy)methoxy]methylidene}cyclohexyl)ethanol* ***(syn-Z* 11h)**, *[1R*(1R*,2E)]-2-benzyloxy-1-(2-{[(2-methoxyethoxy)methoxy]methylidene}cyclohexyl)ethanol* ***(anti-E* 11h)** *and [1R*(1R*,2E)]-2-benzyloxy-1-(2-{[(2-methoxyethoxy)methoxy]methylidene}cyclohexyl)ethanol* ***(anti-Z* 11h)**

IR (thin film) ν cm^{-1} 3 456, 2 924, 1 682, 1 453, 1 177, 1 110, 1 050, 1 027, 909, 848, 678.

^1H NMR (400 MHz, $CDCl_3$, four isomers):

***syn-E* 11h**, δ 7.35–7.26 (m, 5H, Ar-H), *5.97* (br s, 1H, H-1″), 4.81 (br s, 2H, OCH_2O), 4.52 and 4.50 (2d, J = 11.8 Hz, 2H, $ArCH_2O$), 4.02 (m, 1H, H-1), 3.67–3.64 (m, 2H, OCH_2CH_2O), 3.55–3.50 (m, 3H, H-2a and OCH_2CH_2O), 3.36 (s, 3H, CH_3, OCH_3), 3.30 (dd, J = 9.6, 7.6 Hz, 1H, H-2b), 2.55 (dt, J = 13.9, 3.7 Hz, 1H, H-3′a), 2.34 (br d, J = 3.4 Hz, 1H, OH), 2.13–2.05 (m, 2H), 1.74–2.05 (m, 2H), 1.61–1.51 (m, 2H), 1.43–1.35 (m, 1H), 1.31–1.24 (m, 1H).

***syn-Z* 11h**, δ 7.33–7.31 (m, 5H, Ar-H), *6.18* (br s, 1H, H-1″), 4.86 (br s, 2H, OCH_2O), 4.60 and 4.53 (2d, J = 12.1 Hz, 2H, $ArCH_2O$), 3.93 (ddd, J = 8.7, 5.7, 2.5 Hz, 1H, H-1), 3.70–3.68 and 3.54–3.51 (2m, 4H, OCH_2CH_2O), 3.65 (dd, J = 10.0, 2.5 Hz, 1H, H-2a), 3.45 (dd, J = 10.0, 5.7 Hz, 1H, H-2b), 3.36 (s, 3H, CH_3, OCH_3), 2.56 (dt, J = 13.9, 3.9 Hz, 1H, H-3′a), 2.15–2.11 (m, 1H, H-1′), 1.89 (td, J = 12.4, 3.7 Hz, 1H), 1.71–1.61 (m, 2H), 1.55–1.45 (m, 3H), 1.31–1.25 (m, 1H).

***anti-E* 11h**, δ 7.33–7.31 (m, 5H, Ar-H), *6.10* (br s, 1H, H-1″), 4.86 (br s, 2H, OCH_2O), 4.60 and 4.53 (2d, J = 12.1 Hz, 2H, $ArCH_2O$), 3.93 (ddd, J = 8.7, 5.7, 2.5 Hz, 1H, H-1), 3.70–3.68 and 3.54–3.51 (2m, 4H, OCH_2CH_2O), 3.65 (dd, J = 10.0, 2.5 Hz, 1H, H-2a), 3.45 (dd, J = 10.0, 5.7 Hz, 1H, H-2b), 3.36 (s, 3H, CH_3, OCH_3), 2.56 (dt, J = 13.9, 3.9 Hz, 1H, H-3′a), 2.15–2.11 (m, 1H, H-1′), 1.89 (td, J = 12.4, 3.7 Hz, 1H), 1.71–1.61 (m, 2H), 1.55–1.45 (m, 3H), 1.31–1.25 (m, 1H).

***anti-Z* 11h**, δ 7.33–7.31 (m, 5H, Ar-H), *6.01* (br s, 1H, H-1″), 4.86 (br s, 2H, OCH_2O), 4.60 and 4.53 (2d, J = 12.1 Hz, 2H, $ArCH_2O$), 3.93 (ddd, J = 8.7, 5.7, 2.5 Hz, 1H, H-1), 3.70–3.68 and 3.54–3.51 (2m, 4H, OCH_2CH_2O), 3.65 (dd, J = 10.0, 2.5 Hz, 1H, H-2a), 3.45 (dd, J = 10.0, 5.7 Hz, 1H, H-2b), 3.36 (s, 3H, CH_3, OCH_3), 2.56 (dt, J = 13.9, 3.9 Hz, 1H, H-3′a), 2.15–2.11 (m, 1H, H-1′), 1.89 (td, J = 12.4, 3.7 Hz, 1H), 1.71–1.61 (m, 2H), 1.55–1.45 (m, 3H), 1.31–1.25 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$, mixture of four isomers, two isomers assigned):

***syn-E* 11h**, δ 138.1 (C, Ar), 136.8 (C-1″), 128.4, 128.3, 127.7 (C, Ar), 119.7 (C-2′), 95.2 (OCH_2O), 73.6 (C-2), 73.3 ($ArCH_2O$), 71.6 and 67.1 (OCH_2CH_2O), 68.0 (C-1), 58.9 (OCH_3), 41.7 (C-1′), 28.0, 27.0, 22.9, 21.9 (C-3′, C-4′, C-5′, C-6′).

***anti-E* 11h**, δ 138.1 (C, Ar), 137.8 (C-1″), 128.2, 125.5 (C, Ar), 118.0 (C-2′), 95.0 (OCH_2O), 73.2 ($ArCH_2O$), 72.2 (C-2), 71.5 and 67.1 (OCH_2CH_2O), 68.6 (C-1), 58.7 (OCH_3), 41.9 (C-1′), 29.0, 26.7, 22.6, 22.5 (C-3′, C-4′, C-5′, C-6′).

MS (GC/MS, CI, NH_3), m/z 368 ($MH^+ + NH_3$), 262, 168.

Anal calc for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.51; H, 8.57.

• *Hydrolysis of the enol ether function and formation of γ-lactone. Typical procedure*

To a mixture of 5 mL THF and 5 mL 4 N aqueous HCl was added the required enol ether **11a–h**. The resulting solution was stirred at 20 °C for 5 h and extracted twice with diethyl ether. The combined extracts were washed with a saturated aqueous $NaHCO_3$ solution, brine, dried over $MgSO_4$, filtered, and concentrated in vacuo to give the corresponding lactol **14**. This lactol was diluted in 5 mL acetone and treated at 0 °C with a 2 M solution of Jones' reagent. The resulting orange solution was stirred for 15 min at 0 °C and quenched by addition of 2 mL MeOH, partitioned between 25 mL water and 25 mL diethyl ether. The layers were separated and the aqueous phase was extracted with 3 × 25 mL diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was then purified by flash chromatography on silica gel to give pure lactone **15**.

■ *(3R*,4S*,5R*)-3-Phenyl hexahydroisobenzofuran-1(3H)-one* ***(15a*, *αR)***

According to the above procedure, lactone **15a**, αR was obtained in 55% yield from ***syn-E* 11a**.

IR (thin film) ν cm^{-1} 2 934, 2 857, 1 778, 1 496, 1 450, 1 367, 1 327, 1 167, 1 129, 1 025, 987, 915.

^1H NMR (400 MHz, $CDCl_3$) δ 7.39–7.27 (m, 5H, Ar-H), 5.48 (d, J = 4.5 Hz, 1H, H-3), 2.96 (t, J = 5.7 Hz, 1H, H-5), 2.70–2.63 (m, 1H, H-4), 2.27–2.23 (m, 1H), 1.64–1.55 (m, 3H), 1.25–0.98 (m, 3H), 0.86–0.76 (m, 1H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 177.4 (C-1), 136.2 (C, Ar), 128.5, 127.8, 125.3 (C, Ar), 81.8 (C-3), 42.5, 41.2 (C-4, C-5), 23.7 (2 CH_2), 23.2, 22.7 (2 CH_2).

MS (GC/MS, EI) m/z 216 (M^+), 172, 107, 67.

Anal calc for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.59; H, 7.63.

■ *(3R*,4R*,5S*)-3-Phenyl hexahydroisobenzofuran-1(3H)-one* ***(15a*, *βR)***

Lactone **15a**, βR was obtained in 38% yield (two steps) from ***anti-E* 11a**.

IR (thin film) ν cm^{-1} 2 934, 2 856, 1 774, 1 496, 1 450, 1 365, 1 294, 1 236, 1 183, 1 155, 1 124, 1 036, 991, 914.

^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.21 (m, 5H, Ar-H), 5.14 (d, J = 3.4 Hz, 1H, H-3), 2.62 (dd, J = 12.1, 6.2 Hz, 1H, H-5), 2.43–2.37 (m, 1H, H-4), 1.91 (m, 1H), 1.63–1.53 (m, 2H), 1.49–1.24 (m, 4H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 178.5 (C-1), 138.7 (C, Ar), 128.7, 128.2, 125.1 (C, Ar), 83.2 (C-3), 45.2, 38.0 (C-4, C-5), 27.0, 23.1, 23.1, 22.9 (C-6, C-7, C-8, C-9).

MS (GC/MS, CI, NH_3) m/z 234 ($MH^+ + NH_3$), 217 (MH^+).

■ *[3R*(1E),4R*,5S*]-3-(Prop-1-enyl) hexahydroisobenzofuran-1(3H)-one (**15b**, αR)*
Lactone **15b**, αR was obtained in 50% yield (two steps) from ***syn-E* 11b**.

IR (thin film) ν cm^{-1} 2 935, 2 858, 1 772, 1 449, 1 188, 1 131, 970, 913.

^1H NMR (400 MHz, $CDCl_3$) δ 5.83 (dq, J = 15.5, 6.5 Hz, 1H, H-2′), 5.47 (ddq, J = 15.5, 7.5, 1.7 Hz, 1H, H-1′), 4.67 (dd, J = 7.5, 4.5 Hz, 1H, H-3), 2.71 (t, J = 6.0 Hz, 1H, H-5), 2.35–2.31 (m, 1H, H-4), 2.15–2.11 (m, 1H, H-6a), 1.90–1.40 (m, 3H), 1.70 (d, J = 6.5 Hz, 3H, CH_3-2′), 1.30–1.00 (m, 4H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 177.6 (C-1), 131.1 (C-2′), 125.3 (C-1′), 82.1 (C-3), 42.0, 40.7 (C-4, C-5), 23.8, 23.6, 23.1, 22.7 (C-6, C-7, C-8, C-9), 17.7 (CH_3-2′).

MS (GC/MS, EI) m/z 180 (M^+), 165, 107, 79, 67, 54, 39.

Anal calc for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.34; H, 9.06.

■ *(3R*,4R*,5S*)-3-(Cyclohexyl)hexahydroisobenzofuran-1(3H)-one (**15f**, αR)*
Lactone **15f**, αR was obtained in 80% yield (two steps) from ***syn-E* 11f**.

IR ($CDCl_3$) ν cm^{-1} 2 927, 2 853, 1 773, 1 448, 1 200, 1 179, 1 131, 1 021, 978, 943.

^1H NMR (400 MHz, $CDCl_3$) δ 3.80 (dd, J = 10.4, 3.8 Hz, 1H, H-3), 2.66 (t, J = 5.7 Hz, 1H, H-5), 2.38–2.29 (m, 1H, H-4), 2.14 (m, 1H), 2.08–2.00 (m, 1H), 1.90–1.45 (m, 9H), 1.30–1.80 (m, 8H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 177.8 (C-1), 86.2 (C-3), 42.5, 38.2, 36.9 (C-1′, C-4, C-5), 30.6, 28.1, 26.5, 25.6, 25.4, 23.9, 23.1, 22.8, 22.4 (C-6, C-7, C-8, C-9, C-2′, C-3′, C-4′, C-5′, C-6′).

MS (GC/MS, CI, NH_3) m/z 240 ($MH^+ + NH_3$), 223 (MH^+).

Anal calc for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98. Found: C, 74.98; H, 9.89.

■ *(3R*,4R*,5S*)-3-[(2-Benzyloxy)ethyl]hexahydroisobenzofuran-1(3H)-one (**15g**, αR)*
Lactone **15g**, αR was obtained in 66% yield (two steps) from ***syn-E* 11g**.

IR (thin film) ν cm^{-1} 2 934, 2 858, 1 770, 1 452, 1 364, 1 175, 1 103, 911, 732.

^1H NMR (400 MHz, $CDCl_3$) δ 7.33–7.27 (m, 5H, Ar-H), 4.51 (d, J = 11.8 Hz, 1H, ArC*H*O), 4.49 (d, J = 11.8 Hz, 1H, ArC*H*O), 4.50–4.42 (m, 1H, H-3), 3.63–3.59 (m, 2H, H_2-2′), 2.72 (t, J = 6.1 Hz, 1H, H-5), 2.34–2.29 (m, 1H, H-4), 2.20–2.15 (m, 1H, H-6a), 2.00–1.00 (m, 10H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 177.8 (C-1), 138.3 (C, Ar), 129.7, 128.5, 127.7 (C, Ar), 78.9 (C-3), 73.4 (Ar*C*H_2O), 66.9 (C-2′), 42.1, 39.6 (C-4, C-5), 30.4 (C-1′), 25.1, 23.3, 23.0, 22.7 (C-6, C-7, C-8, C-9).

MS (GC/MS, CI, NH_3) m/z 292 ($MH^+ + NH_3$), 275 (MH^+), 202, 106.

■ *(3R*,4S*,5R*)-3-[(2-Benzyloxy)ethyl]hexahydroisobenzofuran-1(3H)-one (**15g**, βR)*
Lactone **15g**, βR was obtained in 54% yield (two steps) from ***anti-E* 11g**.

IR (thin film) ν cm^{-1} 2 927, 2 856, 1 772, 1 450, 1 368, 1 159, 1 102, 982, 917.

^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H, Ar-H), 4.51 (d, J = 11.9 Hz, 1H, ArC*H*O), 4.32 (ddd, J = 8.3, 4.8, 3.4 Hz, 1H, H-3), 3.59 (m, 2H, H_2-2′), 2.67 (dd, J = 11.9, 6.6 Hz, 1H, H-5), 2.25–2.18 (m, 1H, H-4), 2.15–2.10 (m, 1H), 2.00–1.45 (m, 4H), 1.35–1.00 (m, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 179.2 (C-1), 138.5 (C, Ar), 128.5, 127.8 (C, Ar), 80.7 (C-3), 73.4 (Ar*C*H_2O), 66.7 (C-2′), 39.8, 38.6 (C-4, C-5), 33.8 (C-1′), 27.2, 23.8, 23.1, 23.0 (C-6, C-7, C-8, C-9).

MS (GC/MS, CI, NH_3) m/z 292 ($MH^+ + NH_3$), 275 (MH^+).

Anal calc for $C_{17}H_{22}O_3$: C, 74.42; H, 8.08. Found: C, 74.30; H, 7.91.

■ *(3R*,4S*,5R*)-3-[(Benzyloxy)methyl]hexahydroisobenzofuran-1(3H)-one (**15h**, αR)*
Lactone **15h**, αR was obtained in 48% yield (two steps) from ***syn-E* 11h**.

IR (thin film) ν cm^{-1} 2 932, 2 857, 1 773, 1 451, 1 174, 1 124, 1 037, 916, 735, 698.

^1H NMR (400 MHz, $CDCl_3$) δ 7.34–7.28 (m, 5H, Ar-H), 4.60 (d, J = 11.9 Hz, 1H, ArC*H*O), 4.51 (d, J = 11.9 Hz, 1H, ArC*H*O), 4.46 (td, J = 7.0, 4.8 Hz, 1H, H-3), 3.69 (dd, J = 10.4, 7.1 Hz, 1H, H-1′a), 3.62 (dd, J = 10.4, 5.2 Hz, 1H, H-1′b), 2.71 (t, J = 6.0 Hz, 1H, H-5), 2.48–2.40 (m, 1H, H-4), 2.18–2.14 (m, 1H), 1.68–1.48 (m, 4H), 1.27–1.04 (m, 3H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 177.6 (C-1), 137.6 (C, Ar), 128.5, 127.9, 127.8 (C, Ar), 79.9 (C-3), 73.6 (Ar*C*H_2O), 68.2 (C-1′), 41.3, 37.9 (C-4, C-5), 23.4, 22.7, 22.5, 22.4 (C-6, C-7, C-8, C-9).

MS (DI, CI, NH_3) m/z 278 ($MH^+ + NH_3$), 261 (MH^+).

■ *(3R*,4R*,5S*)-3-[(Benzyloxy)methyl]hexahydroisobenzofuran-1(3H)-one (**15h**, βR)*
Lactone **15h**, βR was obtained in 66% yield (two steps) from ***anti-E* 11h**.

IR (thin film) ν cm^{-1} 2 391, 2 856, 1 770, 1 496, 1 452, 1 367, 1 240, 1 158, 1 116, 1 067, 1 028, 917, 738, 700.

^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.26 (m, 5H, Ar-H), 4.54 (d, J = 12.1 Hz, 1H, ArC*H*O), 4.51 (d, J = 12.1 Hz, 1H, ArC*H*O), 4.20 (td, J = 4.2, 3.2 Hz, 1H, H-3), 3.64 (dd, J = 10.7, 4.0 Hz, 1H, H-1′a), 3.58 (dd, J = 10.7, 4.3 Hz, 1H, H-1′b), 2.84 (td, J = 6.8, 4.6 Hz, 1H, H-5), 2.42–2.38 (m, 1H, H-4), 1.97–1.93 (m, 1H, H-6a), 1.82–1.77 (m, 1H), 1.67–1.48 (m, 4H), 1.31–1.19 (m, 2H).

^{13}C NMR (50 MHz, $CDCl_3$) δ 178.7 (C-1), 137.7 (C, Ar), 128.4, 127.9, 127.7 (C, Ar), 82.0 (C-3), 73.7 (Ar*C*H_2O), 70.5 (C-1′), 38.7, 36.8 (C-4, C-5), 27.7, 23.2, 23.1, 22.9 (C-6, C-7, C-8, C-9).

MS (GC/MS, CI, NH_3) m/z 278 ($MH^+ + NH_3$), 261 (MH^+), 108, 91.

Anal calc for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.55; H, 7.91.

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References

1 a) Wani MC, Taylor HL, Wall ME, Coggon P, McPhail AT, *J Am Chem Soc* (1971) 93, 2325-2327
b) ACS Symposium Series 583, *Taxane Anticancer Agents: Basic Science and Current Status*, Georg GI, Chen TT, Ojima I, Vyas DM, eds, American Chemical Society, Washington DC, 1995
2 a) Lavelle F, Guéritte-Voegelein, Guénard D, *Bull Cancer* (1993) 80, 326-338
b) Guénard D, Guéritte-Voegelein F, Potier P, *Acc Chem Res* (1993) 26, 160-167, and references cited therein

3 a) Nicolaou KC, Yang Z, Liu JJ, Ueno H, Nantermet PG, Guy RK, Claiborne CF, Renaud J, Couladouros EA, Paulvannan K, Sorensen EJ, *Nature* (1994) 367, 630-634; Nicolaou KC, Nantermet PG, Ueno H, Guy RK, Couladouros EA, Sorensen EJ, *J Am Chem Soc* (1995) 117, 624-633; Nicolaou KC, Liu JJ, Yang Z, Ueno H, Sorensen EJ, Claiborne CF, Guy RK, Hwang CK, Nakada M, Nantermet PG, ibid (1995) 117, 634-644; Nicolaou KC, Yang Z, Liu JJ, Nantermet PG, Claiborne CF, Renaud J, Guy RK, Shibayama K, ibid (1995) 117, 645-652; Nicolaou KC, Ueno H, Liu JJ, Nantermet PG, Yang Z, Renaud J, Paulvannan K, Chadha R, ibid (1995) 117, 653-659
b) Holton RA, Somoza C, Kim HB, Liang F, Biediger RJ, Boatman PD, Shindo M, Smith CC, Kim S, Nadizadeh H, Suzuki Y, Tao C, Vu P, Tang S, Zhang P, Murthi KK, Gentile LN, Liu JH, *J Am Chem Soc* (1994) 116, 1597-1598; Holton RA, Kim HB, Somoza C, Liang F, Biediger RJ, Boatman PD, Shindo M, Smith CC, Kim S, Nadizadeh H, Suzuki Y, Tao C, Vu P, Tang S, Zhang P, Murthi KK, Gentile LN, Liu JH, *ibid* (1994) 116, 1599-1600
c) Masters JJ, Link JT, Snyder LB, Young WB, Danishefsky S, *Angew Chem, Int Ed Engl* (1995) 34, 1723-1726
d) Wender PA, *The Chemistry–Medecine Continuum: Synthetic, Computer and Biological Studies on Taxol*, French Chemical Society (SFC), Paris, France, 1996

4 Muller B, Delaloge F, den Hartog M, Férézou JP, Pancrazi A, Prunet J, Lallemand JY, Neuman A, Prangé T, *Tetrahedron Lett* (1996) 37, 3313-3316

5 Pereyre M, Quintard JP, Rahm A, *Tin in Organic Synthesis* Butterworths, London, 1987. For a complete review on reactions of allylic metals see Yamamoto Y, Asao N, *Chem Rev* (1993) 2207-2293

6 Ihara M, Suzuki S, Tokunaga Y, Fukumoto K, *J Chem Soc, Perkin Trans I* (1995) 2811-2812

7 Polla M, Frejd T, *Acta Chem Scand* (1993) 47, 716-720

8 a) For general chemistry on α-alkoxy allylic stannanes, see: Pereyre M, Quintard JP, *Pure Appl Chem* (1981) 53, 2401-2417
b) Quintard JP, Elissondo B, Pereyre M, *J Org Chem* (1983) 48, 1559-1560
c) Quintard JP, Dumartin G, Elissondo B, Rahm A, Pereyre M, *Tetrahedron* (1989) 45, 1017-1028

9 a) Pratt AJ, Thomas EJ, *J Chem Soc, Chem Commun* (1982) 1115-1117
b) Jephcote VJ, Pratt AJ, Thomas EJ, *J Chem Soc, Chem Commun* (1984) 800-802
c) Pratt AJ, Thomas EJ, *J Chem Soc, Perkin Trans I* (1989) 93, 1521-1527, ibid 1529-1535

10 a) Marshall JA, Gung WY, *Tetrahedron Lett* (1989) 30, 309-312
b) Marshall JA, Gung W Y, *Tetrahedron* (1989) 45, 1043-1052 and references therein
c) Gung BW, Smith DT, Wolf MA, *Tetrahedron Lett* (1991) 32, 13-16

11 a) Keck GE, Dougherty SM, Savin KA, *J Am Chem Soc* (1995) 117, 6210-6223
b) Denmark SE, Hosoi S, *J Org Chem* (1994) 59, 5133-5135
c) A very recent report deals with *syn*-diastereoselective $BF_3{\cdot}OEt_2$-promoted condensation of 1-(tributylstannylmethyl)cyclohexene with aldehydes: Nichigaichi Y, Ishida N, Nishida M, Takuwa A, *Tetrahedron Lett* (1996) 37, 3701-3704

12 a) For a pertinent review on Lewis-acid-promoted reaction of allyl tin compounds, see: Nishigaichi Y, Takuwa A, Naruta Y, Maruyama K, *Tetrahedron* (1993) 49, 7395-7426 and references cited therein
For other aspects of the chemistry of allylstannanes including asymmetric induction, see:
b) Poli G, Scolastico C, *Chemtracts* (1991) 298-306
c) Marshall JA, ibid (1992) 75-98
d) Thomas EJ, ibid (1994) 207-234

13 All subsequent studies were carried out on racemic materials and stereochemistries refer to relative configurations

14 In the absence of aldehyde, treatment of **11** with 01 equiv $BF_3{\cdot}OEt_2$ followed by direct aqueous acidic treatment afforded the product derived from the hydrolysis of the rearranged stannane **12** in 62% yield (see *Experimental section*)

15 a) Marshall JA, Gung WY, *Tetrahedron Lett* (1989) 30, 2183-2186
The formation as well as the reactivity of γ-alkoxy allylic stannanes was later rationalized:
b) Marshall JA, Gung WY, *Tetrahedron Lett* (1989) 30, 7349-7352
c) Marshall JA, Welmaker GS, Gung WY, *J Am Chem Soc* (1991) 113, 647-656
d) For a recent review on γ-alkoxy allylic stannanes chemistry, see: Marshall JA, *Chem Rev* (1996) 31-47

16 Yamamoto Y, Yatagai H, Ishihara Y, Maeda N, Maruyama K, *Tetrahedron* (1984) 40, 2239-2246

17 a) Shambayati S, Crowe WE, Schreiber SL, *Angew Chem, Int Ed Engl* (1990) 29, 256-272
b) Gung BW, *Tetrahedron Lett* (1991) 32, 2867-2870

18 a) Houk YN, Moses SR, Wu YD, Rondan NG, Jäger V, Schohe R, Fronczek FR, *J Am Chem Soc* (1984) 106, 3880-3882
b) Gung BW, Peat AJ, Snook BM, Smith DT, *Tetrahedron Lett* (1991) 32, 453-456

19 a) Denmark SE, Weber EJ, Wilson TM, Willson TM, *Tetrahedron* (1989) 45, 1053-1065
b) Keck GE, Dougherty SM, Savin KA, *J Am Chem Soc* (1995) 117, 6210-6223

20 Keck GE, Savin KA, Cressman ENK, Abbott DE, *J Org Chem* (1994) 59, 7889-7896

21 A good correlation between covalent radii of Lewis acid metal atoms and observed stereoselectivities has already been suggested to explain the results obtained during intramolecular allylsilane/aldehyde condensations: Denmark SE, Weber EJ, *Helv Chim Acta* (1983) 66, 1655-1660

22 Nakatsuka M, Schreiber SL, *J Synth Org Chem Jpn* (1991) 49, 748-761

23 a) Mikami K, Kawamoto K, Loh TP, Nakai T, *J Chem Soc, Chem Commun* (1990) 1161-1163
b) This paper has been carefully reviewed: Fleming I, *Chemtracts* (1991) 4, 21-25

24 Marshall JA, Jablonowski JA, Luke GP, *J Org Chem* (1994) 59, 7825-7832

25 a) Keck GE, Boden EP, *Tetrahedron Lett* (1984) 25, 1879-1882
b) Keck GE, Abbott DE, *Tetrahedron Lett* (1984) 25, 1883-1886

26 a) Kutney JP, Abdurhaman N, Gletsos C, Le Quesne P, Piers E, Vlattas I, *J Am Chem Soc* (1970) 92, 1727-1735
b) Corey EJ, Suggs JW, *Tetrahedron Lett* (1975) 2647-2650