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Regio- and stereochemical aspects in the synthesis of homoallylic alcohols from benzoins and their iodocyclisation to 2,3-diphenyltetrahydrofurans

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Abstract—Indium mediated allylation, crotylation and cinnamylation of benzoins and its substituted derivatives in THF–H_2O (2/1) provide a range of homoallylic alcohols. In general, the benzoins undergo allylation and crotylation in a sluggish manner compared to those observed earlier in the case of α-hydroxy aldehydes and are significantly affected by the electronic features of both the benzoin and indium organometallic reagent. The reactions exhibit higher order of diastereoselectivities than those observed for α-hydroxy aldehydes. The cinnamylation though proceeds in a highly diastereoselective manner but is restricted to only benzoin and 4,4′-dichlorobenzoin. The homoallylic alcohols undergo I_2 mediated intramolecular diastereoselective cyclization to provide 2,3-diphenyltetrahydrofuran derivatives. The relative stereochemistries in tetrahydrofurans and homoallylic alcohols have been assigned by coupling constants, NOE experiments and in one case by X-ray crystallography.

1. Introduction

The allylation of carbonyl compounds with allyl organometallic reagents constitutes a simple approach for the synthesis of homoallylic alcohols, versatile synthons in organic synthesis.[1] The stability of indium metal in water, ease in generation of allyl indium reagents under anhydrous conditions and in situ generation under aqueous Barbier type conditions; the lower basicity and thus the higher stability of allylindium reagents in the presence of water and other proton donor functionalities such as OH, COOH; the applicability even in the presence of NO_2, CN, ester functional groups, have highlighted the superiority of allyl indium reagents[2] over conventional organometallic reagents.[3] The environment friendly reaction conditions and the higher reactivities in these multi-component reactions in aqueous media are added advantages of indium mediated allylation reactions.[4]

The pioneering investigations of Paquette et al.[5] on the stereochemical outcome of allylation of α-hydroxy aldehdyes, in general, show the participation of Cram's chelation model and allylic anions preferably add from the sterically less hindered face to provide *syn* homoallylic alcohols. The presence of water does not inhibit the operation of chelation control. The choice of the solvent, different additives and pH of the reaction medium also affect the diastereoselective outcome of the reaction. However, due to poor reactivities of ketones compared to aldehydes towards nucleophiles, these investigations have been limited to allylation of hydroxycyclohexanones[6] and carbohydrates[7] with only allyl bromide.

The present work is aimed to unravel the regio- and diastereochemical aspects in allylation of benzoins—the acyclic α-hydroxyketones[8] with allyl and substituted allyl bromides. The presence of two aryl rings at adjacent carbons make them attractive synthons for α,β-diaryl heterocycles—an essential structural feature in many bioactive molecules especially COX-2 inhibitors.[9]

The findings show that benzoins, in general, undergo indium mediated allylation and crotylation in a sluggish manner than those observed earlier in the case of α-hydroxy aldehydes. The presence of electron-withdrawing groups on the aryl rings facilitates the allylation and the presence of electron-donating groups retards the allyl transfer. The cinnamylation proceeds in a highly diastereoselective manner (>98:2) with benzoin and 4,4′-dichlorobenzoin. Homoallylic alcohols thus obtained undergo I_2 mediated diastereoselective intramolecular cyclizations to give

Keywords: Benzoins; Indium; Homoallylic alcohols; Iodocyclisation; Regioselective; Diphenyltetrahydrofurans.
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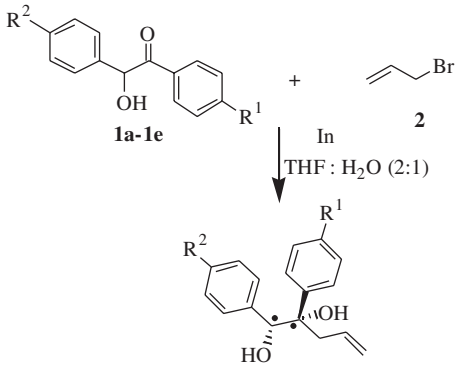
2,3-diaryltetrahydrofurans. The configurations of tetrahydrofurans and homoallylic alcohols have been assigned by NOE experiments and by X-ray crystallography in one case.

2. Results and discussion

2.1. Diastereoselective allylation with allyl bromide: generation of one new chiral center

A solution of **1a**, allyl bromide **2** and indium metal (suspension) (1:1.5:1) in THF–H_2O (2/1) on stirring at 30 ± 2 °C for 6–8 h, after usual work-up and chromatography provided (1*R**,2*S**)-**3a** (92%), mp 95 °C, (lit.[10] mp 96–97 °C (Scheme 1). This procedure offers a convenient alternative to similar allylation performed through tetraallyltin.[10] In order to evaluate the contribution of electronic features on the reactivity and diastereoselectivity of allylation on benzoins, the substituted benzoin derivatives **1b–1e** were subjected to indium mediated allylation under Barbier type conditions. Benzoins **1b–1d** on allylation gave homoallylic alcohols **3b–3d** with diastereoselectivities >99:1 (Scheme 1, Table 1). *N*,*N*-Dimethylbenzoin **1e** did not undergo indium mediated allylation and even on performing the reaction at 50 °C, the starting **1e** (~50%) was recovered.



For 1, 3 (a) $R^1=R^2=H$; (b) $R^1=R^2=Cl$; (c) $R^1=OCH_3$, $R^2=H$; (d) $R^1=R^2=OCH_3$; (e) $R^1=N(CH_3)_2$, $R^2=H$

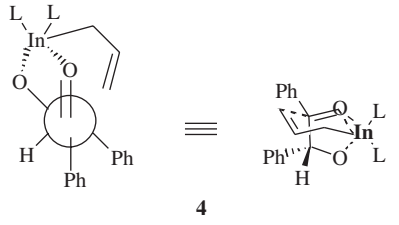
Scheme 1.

Table 1. Diastereoselective allylation of benzoins **1a–1e**

Entry	R^1	R^2	Product	Time (h)	dr	Yield (%)
1	H	H	**3a**	7–8	>99:1	92
2	Cl	Cl	**3b**	4–5	>99:1	45
3	OCH_3	H	**3c**	12–14	>99:1	69
4	OCH_3	OCH_3	**3d**	12–14	>99:1	72
5	$N(CH_3)_2$	H	**3e**	24	No reaction	

The time required for allylation of benzoins **1a–1e** is considerably affected by the nature of the substituent on the aryl ring and is by and large in parallel with the electron-densities available on the carbonyl carbon. 4,4′-Dichlorobenzoin **1b** undergoes allylation faster than benzoin **1a** and in the case of anisoin **1d** and benzanisoin **1c**, possessing electron-donating group (OMe) the allylation takes a longer time (Table 1, entry 1–4). The presence of a strong electron-donating group [$N(CH_3)_2$] leads to complete inhibition of the allyl transfer even at elevated temperature (50 °C). A comparison of reaction times required for allylation of benzoins with those of α-hydroxyaldehydes[5] shows that benzoins (4–14 h) take more time for completion of the reaction than taken by α-hydroxyaldehydes (2–4 h). These results are in agreement with the known higher reactivities of aldehydes compared to ketones towards nucleophilic addition reactions. Interestingly, the lower reactivities of benzoins towards indium mediated allylation than observed for α-hydroxyaldehydes, results in high (>99:1) diastereoselectivities.

In these reactions, the formation of *syn* products can be visualized on the basis of classic Cram's chelation model **4** (Scheme 2). The ability of the indium cation to lock the hydroxy carbonyl substrates conformationally prior to the nucleophilic attack is indicative that co-ordination to the substrate indeed overcomes the solvation forces.

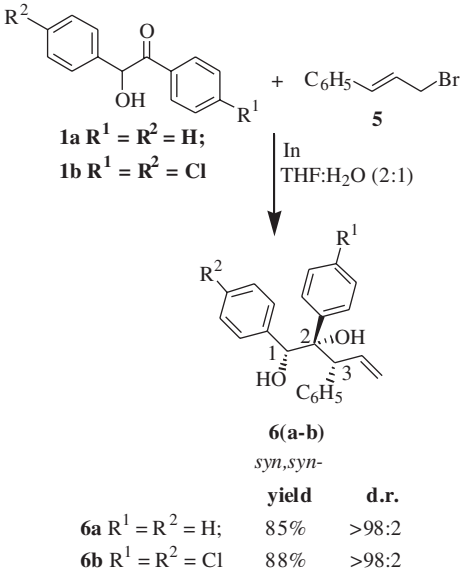


Scheme 2.

2.2. Diastereoselective allylation with substituted allyl bromides: generation of two new chiral centers

The allylic anions generated from substituted allyl bromides are unsymmetrical and the documented preferred carbon–carbon bond formation in the case of aldehydes from the more substituted carbon results in the generation of two new chiral centers.[2] In the case of benzoins, it would lead to formation of homoallylic alcohols with three chiral centers resulting in possible formation of four diastereomers. In order to evaluate the regio- and stereoselective aspects in allylation of benzoins **1a–1d**, indium mediated Barbier type allylations with crotyl bromide, cinnamyl bromide and ethyl 4-bromocrotonate were performed.

Stirring of a solution of benzoin **1a** with cinnamyl bromide (**5**) in THF–H_2O (2/1) at 0 °C containing fine flakes of indium gave a pale yellow liquid (85%), M^+ *m/z* 330 (Scheme 3). It's ^1H NMR spectrum shows a singlet at δ 3.02 (PhC*H*OH), doublet at δ 4.14 (PhC*H*) and multiplet at δ 5.11–5.17 (=CH_2), dt at 6.15 (1H, =CH) and multiplet at 7.02–7.56 (15H, ArH). These spectral data along with the ^{13}C NMR spectrum assigns structure **6a** for this compound. Therefore, cinnamylation of **1a** proceeds in a complete regio- and diastereoselective manner and provides only the γ-addition product. The presence of only one set of signals in the ^1H and ^{13}C NMR spectra of **6a** indicates that only one

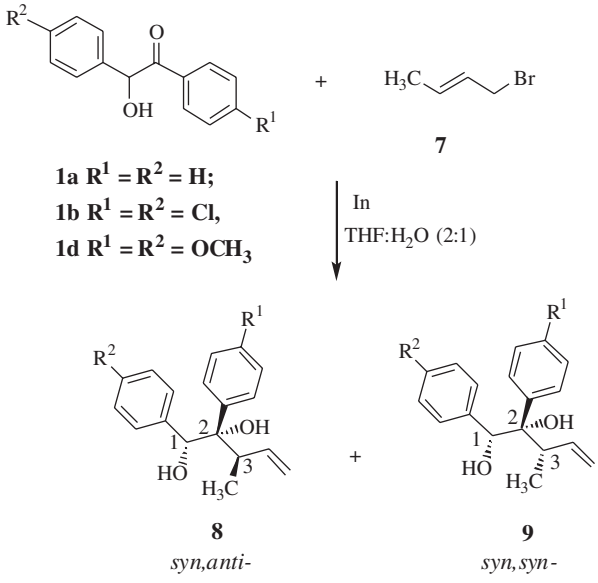


	yield	d.r.
6a $R^1 = R^2 = H$;	85%	>98:2
6b $R^1 = R^2 = Cl$	88%	>98:2

Scheme 3.

diastereomer is formed. On the basis of NOE experiments on its iodocyclized tetrahydrofuran derivatives **14a** and **15a**, it has been assigned as *syn*,*syn*-addition product-(1*R**,2*S**,3*R**)-1,2,3-triphenylpent-4-ene-1,2-diol (**6a**). **1b** also underwent diastreoselective cinnamylation to provide **6b**. However, the electron rich benzoins **1c** and **1d** failed to react with cinnamyl bromide under these conditions.

In the case of crotyl bromide, the minimum steric requirement inherited by the CH_3 group provides a good opportunity to test the diastereoselectivity of the system under investigation. The reaction of benzoin **1a** with crotyl bromide in THF–H_2O (2/1) at 0 °C gave a yellow liquid (78% yield) (Scheme 4). Its ^1H NMR spectrum shows two distinct signals each for CH_3, CH and =CH protons in a 64:36 ratio. The two CH_3 doublets appear at δ 0.93 and 1.06 and could be assigned to CH_3 attached to the sp^3 hybridized carbon. The absence of a signal due to the methyl group between δ 1.5–2.5 shows the non-formation of α-addition product. Therefore, the crotylation too proceeds in a highly regioselective manner to provide only the γ-addition products. Further, out of the possible four diastreomers only two are formed. The two diastereomers could not be separated but relative configurations at the chiral centers have been assigned on the basis of NOE experiments on their iodocyclized products **12a** and **13a**. The major diastereomer has been assigned the configurations (1*R**,2*S**,3*R**)-**8a** and found to be *syn*,*anti*-addition product and minor, which is a *syn*,*syn*-addition product has been assigned configurations (1*R**,2*S**,3*S**)-**9a**. Similarly, **1b** and **1d** on crotylation gave **8b**+**9b** and **8c**+**9c** (Table 2). Amongst these pairs of diastereomers **8a**–**8c** and **9a**–**9c**, the methine vinylic proton (=CH) of *syn*,*anti*-addition products **8** appear downfield at δ 6.07–6.12 in comparison with that of the *syn*,*syn*-addition products **9** (δ 5.78–5.92). These results are in consonance with earlier reported downfield appearance of methine vinylic proton in *anti*-addition product compared to in *syn*-addition product.[11] The allylation of **1a**–**1d** with ethyl 4-bromocrotonate failed to occur even at elevated temperature (50 °C) and only unreacted **1a**–**1d** could be isolated.



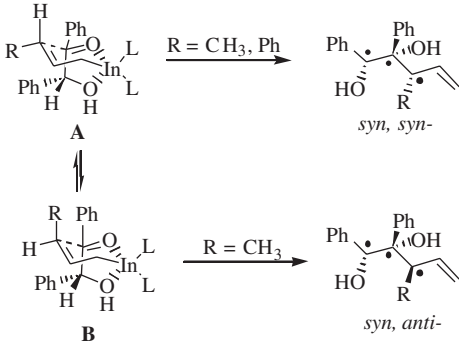
		yield	dr
For 8 and 9	(a) $R^1 = R^2 = H$	78%	64:36
	(b) $R^1 = R^2 = Cl$	74%	64:36
	(c) $R^1 = R^2 = OCH_3$	71%	78:22

Scheme 4.

Table 2. Diastereoselective allylation of benzoins **1** with substituted allyl bromides

Entry	Allyl bromide	Benzoin	Time (h)	Product (*syn*,*syn*:*syn*,*anti*)	Yield (%)
1	5	**1a**	24	**6a** (98:2)	85
2	5	**1b**	4–5	**6b** (98:2)	88
3	7	**1a**	3–4	**8a**+**9a** (64:36)	78
4	7	**1b**	1–2	**8b**+**9b** (64:36)	71
5	7	**1d**	5–6	**8c**+**9c** (78:22)	74

The allylation reactions of **1a** with cinnamyl and crotyl bromide also proceed through Cram's chelation model. The reaction of benzoin **1a** and **1b** with cinnamyl bromide proceed through transition state **A** resulting in the formation of *syn*,*syn*-addition product in which the cinnamyl anion is transferred to the carbonyl carbon from less hindered π-face. However, crotylation of **1a**, **1b** and **1d** preferentially proceeds through transition state **B**, resulting in formation of the *syn*,*anti*- as the major products (Scheme 5).

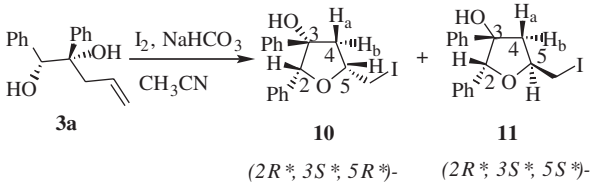


Scheme 5.

The comparison of these results with crotylation of 2-hydroxypropanal shows that whereas in the latter case the mixture of *syn*,*syn*-, *syn*,*anti*- and *anti*,*anti*-addition products is formed,[5d] the crotylations of benzoins provide only *syn*,*syn*- and *syn*,*anti*-addition products.

2.3. Diastereoselective conversion of homoallylic alcohols to 2,3-diphenyltetrahydrofurans 10–15

Stirring a mixture of **3a**, I_2 and $NaHCO_3$ in dry CH_3CN for 72 h after usual work up gave a mixture of two diastereomers in the ratio 80:20 (^{1}H NMR integration) (Scheme 6). The fast moving component (minor 8%) in its ^{1}H NMR spectrum shows two 1H double doublets at δ 2.48 and 2.78 (H-4), a doublet at δ 3.63 (CH_2I), 1H singlet at δ 5.29 (H-2), 1H multiplet at δ 4.57–4.72 (H-5) and 10H multiplet at δ 7.04–7.39. The assignment of the signals has been carried out on the basis of decoupling experiments and ^{1}H–^{13}C COSY spectrum. The relative configurations at C-2 and C-3 carbons are predefined by ^{1}H NMR and X-ray structure of **3a**, and relative configurations at C-2 and C-5 carbons could be assigned on the basis of NOE experiments. The observation of positive NOE at H-4a and H-5 on irradiating H-2 and NOE at H-2, H-5 on irradiating H-4a indicates the presence of H-2, H-4a and H-5 protons on the same side of tetrahydrofuran ring. On the basis of these results the minor component has been assigned the structure (2*R**,3*S**,5*R**)-5-iodomethyl-2,3-diphenyl-tetrahydro-furan-3-ol (**10**) (Fig. 1).



Scheme 6.

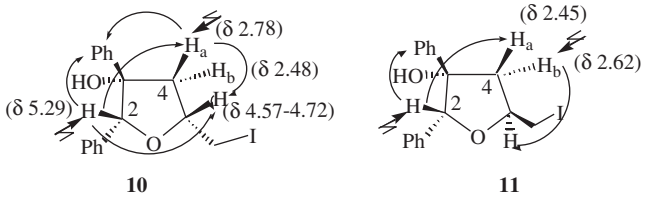


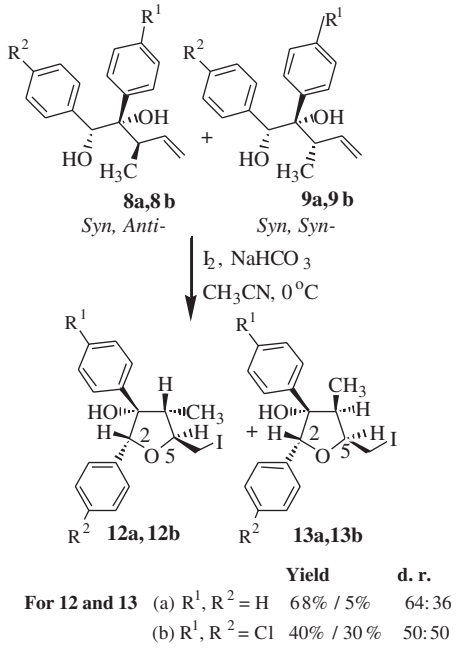
Figure 1. The relative stereochemistries in **10** and **11** from NOE experiments.

The slow moving component (major diastereomer, 32%) in its ^{1}H NMR spectrum shows two 1H double doublets at δ 2.45 and 2.62 (CH_2-4) and two double doublets at δ 3.51 and 3.61 (CH_2I), 1H singlet at δ 5.53 (H-2) and multiplet at δ 4.55–4.60 (H-5) along with aromatic protons. The presence of NOE at H-4a and its absence at H-5 on irradiating H-2 assigns the structure (2*R**,3*S**,5*S**)-5-iodomethyl-2,3-diphenyl-tetrahydro-furan-3-ol (**11**) to this isomer. Therefore, **3a** undergoes regioselective iodocyclisation to provide only tetrahydrofuran derivatives. However, the cyclization proceeds with moderate diastereselectivity to provide two diastereomers in 80:20 ratio. Since, diastereoselectivities in iodocyclisations of **3a** are affected by the temperature and the polarity of the solvent,[12] in order to improve diastereoselectivities, the iodocyclisation was performed at different temperatures using solvents with varied polarities. It was observed that lowering the reaction temperature to 0 °C increased the overall yield to 90% and marginally improved the diastereoselectivity from 80:20 to 86:14. However, on performing iodocyclisation in CH_2Cl_2 diastereoselectivity decreased and in toluene both yield and diastereoselectivity was lowered (Table 3).

Table 3. Effect of solvent and temperature on iodocyclisation of **2a**

S.no.	Solvent	Temperature (°C)	10:11	Yield (%)
1	CH_3CN	30	20:80	40
2	CH_3CN	0	14:86	90
3	CH_2Cl_2	0	25:75	87
4	Toluene	0	20:80	75

Iodocyclisation of a 64:36 mixtures of **8a** and **9a** in CH_3CN at 0 °C provides a 64:36 mixtures of two diastereomers (Scheme 7). The diastereomeric ratio has been calculated on the basis of integration of 1H singlets due to H-2 protons of two diastereomers at δ 5.57 (major) and 5.94 (minor). The formation of only two compounds indicates that **8a** and **9a** underwent highly regio- and stereoselective iodocyclisation to provide one product each, **12a** and **13a**, respectively. Similarly, iodocyclisation of mixture of **8b**+**9b** in CH_3CN at 0 °C gave **12b** and **13b** in 1:1 ratio (Scheme 7). In case of **12a–12b**, $J_{H4,H5}$=9.3 Hz and in **13a–13b** $J_{H4,H5}$=4.5 Hz show that H-4 and H-5 are placed trans to each other in **12** and cis to each other in **13**. The relative stereochemistries at C-2, C-4 and C-5 carbons in **12a–12b** and **13a–13b** have been assigned on the basis of coupling constants, NOE experiments and by X-ray structure in the case of **12b**.



Scheme 7.

The X-ray crystal structure of **12b** (Fig. 2) shows that CH_2I, C(5) Ph and C(12) H are placed on one face of the five member ring whereas C(12) Ph, OH and CH_3 are on the other face of the five member ring. As a result the protons at

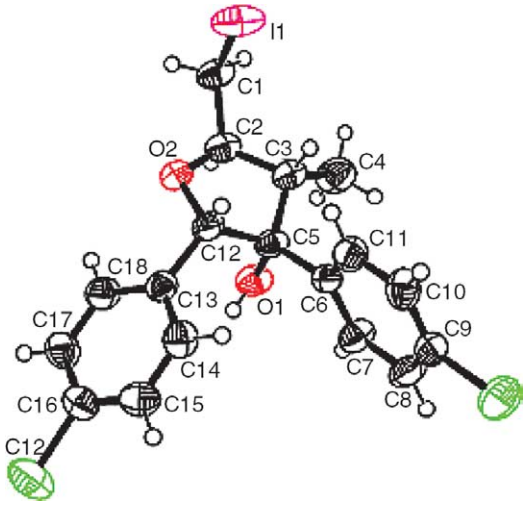
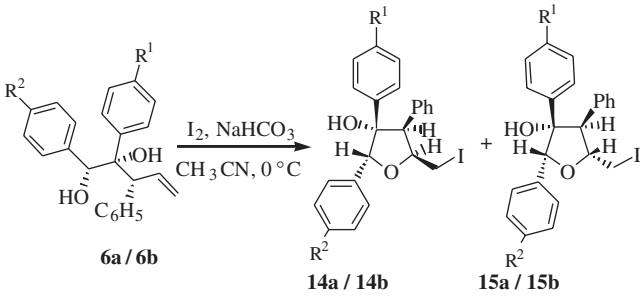


Figure 2. The ORTEP view (50% ellipsoid) of **12b**.

C(2) and C(3) carbons are placed trans to each other. C(12)–O(2)–C(2)–C(3) atoms of the tetrahydrofuran ring are by and large in the same plane and C(5) carbon bearing phenyl and hydroxyl groups moves out of plane making the five member ring as an envelope type structure. All atoms of Cl-Ph rings are in one plane. Cl-Phenyl at the C(5) carbon is almost perpendicular to the plane of five member ring. The results of NOE experiments on **12b** are consistent with the X-ray structure.

Iodocyclisation of **6a** gave a 70:30 mixture of two diastereomers **14a** and **15a** (Scheme 8). ^{1}H NMR of this mixture shows distinct signals for all the protons except aryl protons. The assignment of the signals to specific protons has been made on the basis of 1H decoupling experiments. In the minor component, decoupling of 1H dt at δ 4.87 converts doublets at δ 3.82 and 3.61 into singlets. In the major component, decoupling of H-5 (ddd at δ 5.46) converts H-4 doublet (δ 3.64) into singlet and two double doublets due to CH_2I (δ 3.19 and 3.51) into two doublets. The assignment of relative stereochemisteries at various carbons is made on the basis of NOE experiments. In major diastereomer, irradiation of H-5 (ddd at δ 5.46) shows 14.2% NOE enhancement of H-4 (δ 3.64) and irradiation of H-2 singlet (δ 6.11) shows 9.2% NOE enhancement of 1H of CH_2I (δ 3.51) (Fig. 3). Therefore, H-2 and CH_2I



		yield	d. r.
For **14** and **15**	(a) $R^1 = R^2 = H$	80%	70:30
	(b) $R^1 = R^2 = Cl$	75%	53:47

Scheme 8.

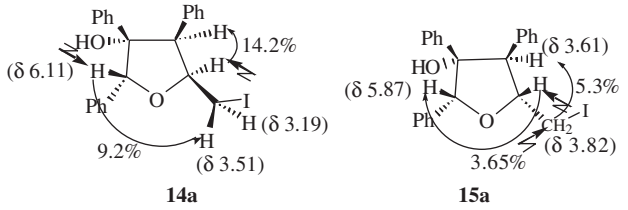


Figure 3. The relative stereochemistries in **14a** and **15a** from NOE experiments.

are on same face and H-4 and H-5 are on the other face of tetrahydrofuran ring and assign structure (2*R**,3*S**,4*S**,5*S**)-**14a** to the major component.

In the case of minor diastereomer, irradiation of H-5 (dt, δ 4.87) shows 3.65% NOE enhancement of H-2 and irradiation of CH_2I (d, δ 3.82) shows 5.34% NOE enhancement of CH-4 (δ 3.61). Therefore, H-5 and H-2 are on same face of the furan ring and CH_2I and H-4 are on the other face of the furan ring (Fig. 3). These spectral data assign structure (2*R**,3*S**,4*S**,5*R**)-**15a** to the minor component. Similarly, **6b** on iodocylisation gave non-separable mixture of **14b** and **15b**.

3. Conclusion

The benzoins in indium mediated allylation reactions follow Cram's chelation model to provide mainly or only *syn*-addition products. The reactions are more sluggish than for α-hydroxy aldehdyes but exhibit higher regio- and diastereoselectivity and are significantly affected by the electron-densities available on the ketone carbon and the reactivity of the allylic anion. The more reactive allylic and crotyl anions add on the benzoins **1a**–**1d**, but cinnamyl anion adds on electron-deficient benzoins **1a** and **1b** only and least reactive ethyl crotonate anion fails to react with all the benzoins. The diastereoselectivities in iodine mediated intramolecular cyclizations are significantly affected by the substituent at C-3 of the homoallylic alcohols. Also the presence or absence of a substituent at C-4 carbon do not affect the preffered relative stereochemistries at C-2 and C-5 carbons and in the case of the only or the major iodocyclized tetrahydrofuran derivatives C2-Ph and C-5 CH_2I are placed on the opposite face.

4. Experimental

4.1. General details

Melting points were determined in capillaries. ^{1}H and ^{13}C NMR spectra were run on JEOL 300 and 75 MHz NMR, respectively, using $CDCl_3$ as solvent. Chemical shifts are given in ppm with TMS as an internal reference. *J* values are given in Hertz. Chromatography was performed with silica 100–200 mesh and the reactions were monitored by thin-layer chromatography (TLC) with silica plates coated with silica gel HF-254.

4.2. General procedure

Procedure A. Barbier type conditions: the carbonyl compound **1** (5 mmol), allyl bromide (7.5 mmol), indium metal (5 mmol) were taken in THF–H_2O (2/1) mixture (10 mL) and the reaction mixture was stirred at 30+2 °C till the indium metal dissolved. The turbid reaction mixture was treated with 4 N HCl and was extracted with $CHCl_3$ (3× 25 mL). The organic phase was dried over Na_2SO_4. The solvent was distilled off and the residue was column chromatographed (silica gel, 60–120 mesh) to isolate pure homoallylic alcohol. The reactions of **1** with cinnamyl and crotyl bromides were performed at 0 °C.

4.2.1. (1*R,2*S**)-1,2-Diphenyl-pent-4-ene-1,2-diol (3a).** Procedure A. 1.17 g, 92%, white solid, mp 95 °C ($CHCl_3$); M^+ *m/z* 237 (M^+-OH); ^1H NMR ($CDCl_3$): δ 2.58 (s, 1H, OH, exchanges with D_2O), 2.59 (s, 1H, exchanges with D_2O, OH), 2.77 (dd, $J_1=14.1$ Hz, $J_2=8.7$ Hz, 1H, 1H of CH_2), 2.93 (dd, $J_1=14.1$ Hz, $J_2=5.7$ Hz, 1H, 1H of CH_2), 4.80 (s, 1H, CH), 5.06–5.26 (m, 2H, $=CH_2$), 5.50–5.63 (m, 1H, =CH), 6.96–7.23 (m, 10H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 42.4 (CH_2), 78.3 (C), 80.4 (CH), 119.8 (CH_2), 126.5 (CH), 126.9 (CH), 127.4 (CH), 127.6 (CH), 127.7 (CH), 133.2 (CH), 139.2 (C), 141.4 (C); IR ν_{max} (KBr): 3469 (OH), 3552 (OH) cm^{-1}. (Found C 80.1%, H 6.9% $C_{17}H_{18}O_2$ requires C 80.28%, H 7.13%).

4.2.2. (1*R,2*S**)-1,2-Bis(4-chloro-phenyl)-pent-4-ene-1,2-diol (3b).** 726 mg, 45%, white solid, mp 92 °C, FAB mass M^+ *m/z* 323, 325, 327 (100:69:1) (M^+); ^1H NMR ($CDCl_3$): δ 2.61 (br s, 2H, 2×OH), 2.71 (dd, $J_1=14$ Hz, $J_2=8.7$ Hz, 1H, 1H of CH_2), 2.87 (dd, $J_1=14$ Hz, $J_2=5.4$ Hz, 1H, 1H of CH_2), 4.72 (s, 1H, CH), 5.12–5.21 (m, 2H, $=CH_2$), 5.49–5.59 (m, 1H, CH), 6.92–7.26 (m, 8H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 42.5 (CH_2), 77.9 (C), 79.6 (CH), 120.4 (CH_2), 127.7 (CH), 127.9 (CH), 129.1 (CH), 131.5 (CH), 132.5 (CH), 133.0 (C), 133.5 (C), 137.6 (C) 139.8 (C); IR ν_{max} (KBr): 3348 (OH), 3421 (OH) cm^{-1}. (Found C 63.0%, H 4.7% $C_{17}H_{16}O_2Cl_2$ requires C 63.17%, H 4.99%).

4.2.3. (1*R,2*S**)-1-(4-Methoxy-phenyl)-2-phenyl-pent-4-ene-1,2-diol (3c).** Procedure A. 979 mg, 69%, light yellow liquid, FAB mass M^+ *m/z* 284 (M^+); ^1H NMR ($CDCl_3$): δ 2.53 (br s, 1H, OH, exchanges with D_2O), 2.57 (br s, 1H, OH, exchanges with D_2O), 2.71 (dd, $J_1=14$ Hz, $J_2=8.7$ Hz, 1H, 1H of CH_2), 2.90 (dd, $J_1=14$ Hz, $J_2=5.4$ Hz, 1H, 1H of CH_2), 3.77 (s, 3H, OCH_3), 4.81 (s, 1H, CH), 5.08–5.19 (m, 2H, $=CH_2$), 5.51–5.63 (m, 1H, CH), 6.74 (d, $J=8.7$ Hz, 2H, ArH), 6.99–7.21 (m, 7H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 42.3 (CH_2), 55.1 (CH_3), 78.1 (C), 80.5 (CH), 112.9 (CH), 119.7 (CH_2), 127.4 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 127.9 (CH), 128.4 (CH), 130.1 (CH), 132.3 (CH), 133.2 (CH), 133.3 (CH), 133.4 (C), 139.3 (C), 158.4 (C); IR ν_{max} ($CHCl_3$): 3390 (OH), 3430 (OH) cm^{-1}. (Found C 76.5%, H 6.90% $C_{18}H_{20}O_3$ requires C 76.03%, H 7.09%).

4.2.4. (1*R,2*S**)-1,2-Bis(4-methoxy-phenyl)-pent-4-ene-1,2-diol (3d).** 1.13 g, 72%, white solid, mp 90 °C ($CHCl_3$); FAB mass M^+ *m/z* 314 (M^+); ^1H NMR ($CDCl_3$): δ 2.59 (br s, 2H, 2×OH, exchanges with D_2O), 2.68 (dd, $J_1=14$ Hz, $J_2=8.7$ Hz, 1H, 1H of CH_2), 2.85 (dd, $J_1=14$ Hz, $J_2=5.4$ Hz, 1H, 1H of CH_2), 3.73 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 4.74 (s, 1H, CH), 5.07–5.18 (m, 2H, $=CH_2$), 5.52–5.63 (m, 1H, CH), 6.67 (d, $J=9$ Hz, 2H, ArH), 6.72 (d, $J=9$ Hz, 2H, ArH), 6.91 (d, $J=9$ Hz, 2H, ArH), 7.03 (d, $J=9$ Hz, 2H, ArH); the decoupling of 2H doublet at δ 6.91 converts doublet at δ 6.67 into singlet and decoupling of doublet at δ 7.03 converts doublet at δ 6.72 into singlet. This indicates that two doublets at δ 7.03 and 6.72 and two doublets at δ 6.67 and 6.91 are due to protons of the same ring. ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 42.4 (CH_2), 55.0 (OCH_3), 55.4 (OCH_3), 78.1 (C), 80.1 (CH), 112.7 (CH), 112.8 (CH), 119.5 (CH_2), 127.8 (CH), 128.9 (CH), 131.5 (C), 133.4 (CH), 133.5 (C), 158.3 (C), 158.9 (C); IR ν_{max} (KBr): 3369 (OH), 3404 (OH) cm^{-1}. (Found C 72.30%, H 6.98% $C_{19}H_{22}O_4$ requires C 72.59%, H 7.05%).

4.2.5. (1*R,2*S**,3*R**)-1,2,3-Triphenyl-pent-4-ene-1,2-diol (6a).** 1.40 g, 85%, pale yellow liquid, FAB mass M^+ *m/z* 330 (M^+); ^1H NMR ($CDCl_3$): δ 3.02 (br s, 2H, 2×OH, exchanges with D_2O), 4.14 (d, $J=8.7$ Hz, 1H, CHPh), 5.11–5.17 (m, 2H, $=CH_2$), 5.22 (s, 1H, CHOH), 6.15 (dt, $J_1=18$ Hz, $J_2=9$ Hz, 1H, =CH), 7.02–7.56 (m, 15H, ArH). The decoupling of dt at δ 6.15 converts doublet at δ 4.14 into singlet and multiplet at δ 5.10–5.16 into broad singlet. ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 58.2 (CH), 76.9 (CH), 80.8 (C), 117.9 (CH_2), 126.9 (CH), 127.1 (CH), 127.4 (CH), 127.5 (CH), 128.4 (CH), 128.6 (CH), 130.0 (CH), 130.3 (CH), 138.2 (CH), 139.6 (C), 139.9 (C), 140.8 (C); IR ν_{max} ($CHCl_3$): 3446 (OH), 3523 (OH) cm^{-1}. (Found C 82.75%, H 6.23% $C_{23}H_{22}O_2$ requires C 83.60%, H 6.71%).

4.2.6. (1*R,2*S**,3*R**)-1,2-Bis(4-chloro-phenyl)-3-phenyl–pent-4-ene-1,2-diol (6b).** 1.76 g, 88%, white solid, mp 72 °C ($CHCl_3$); FAB mass M^+ *m/z* 399 (M^+), 401, 403 (100:69:1) (M^+);^1H NMR ($CDCl_3$): δ 3.01 (br s, 1H, OH, exchanges with D_2O), 4.10 (d, $J=9.3$ Hz, 1H, CHPh), 5.13–5.18 (m, 3H, $=CH_2$, C*H*OH), 5.85 (br s, 1H, exchanges with D_2O), 6.10 (ddd, $J_1=13.8$ Hz, $J_2=9$ Hz, $J_3=6.3$ Hz, 1H, =CH), 6.97–7.41 (m, 13H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 58.3 (CH), 75.4 (CH), 76.1 (CH), 80.4 (C), 118.5 (CH_2), 127.2 (CH), 130.4 (CH), 131.2 (CH), 134.7 (C), 137.5 (CH), 138.2 (C), 138.9 (C), 139.2 (C), 140.7 (C); IR ν_{max} (KBr): 3421 (OH), 3434 (OH) cm^{-1}. (Found C 68.9%, H 4.9% $C_{23}H_{20}O_2Cl_2$ requires C 69.18%, H 5.05%).

4.2.7. (1*R,2*S**,3*R**)-3-Methyl-1,2-diphenyl-pent-4-ene-1,2 diol (8a)+(1*R**,2*S**,3*S**)-3-methyl-1,2-diphenyl-pent-4-ene-1,2 diol (9a).** 998 mg, 78%, pale yellow liquid, FAB mass M^+ *m/z* 268 (M^+); ^1H NMR ($CDCl_3$): δ 0.90 (d, $J=6.6$ Hz, 3H, $CH_{3\text{-major}}$), 1.02 (d, $J=6.9$ Hz, 3H, $CH_{3\text{-minor}}$), 1.25 (br s, 2H, 2×OH, exchanges with D_2O), 2.92–2.99 (m, 1H, CH_{major}), 3.02–3.09 (m, 1H, CH_{minor}), 5.12–5.34 (m, 3H, 2H of $=CH_2$, 1H of CHOH), 5.86 (ddd, $J_1=18.3$ Hz, $J_2=9.9$ Hz, $J_3=7.8$ Hz, 1H, $=CH_{minor}$), 6.13 (ddd, $J_1=19.2$ Hz, $J_2=9.0$ Hz, $J_3=8.1$ Hz,1H, $=CH_{major}$), 6.98–7.19 (m, 10H, ArH); decoupling of doublet at δ 0.90 due to $CH_{3\text{-major}}$ converts multiplet at δ 2.92–2.99 into doublet while decoupling of d at δ 1.06 converts multiplet at 3.02–3.09 into doublet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 14.2 ($CH_{3\text{-minor}}$), 16.2 ($CH_{3\text{-major}}$), 44.6 ($CH_{\text{-minor}}$), 45.2 (CH_{major}), 76.6 (CH), 77.9 (CH), 80.6 ($C_{\text{-minor}}$),

80.8 ($C_{\text{-major}}$), 116.4 ($CH_{2\text{-minor}}$), 116.8 ($CH_{2\text{-major}}$), 126.6 (CH), 126.7 (C), 126.8 (CH), 127.1 (CH), 127.2 (CH), 127.4 (CH), 127.5 (C), 127.5 (CH), 127.6 (CH), 127.8 (CH), 127.9 (CH), 140.3 (CH), 141.1 (CH); IR ν_{max} ($CHCl_3$): 3479 (OH), 3492 (OH) cm^{-1}. (Found C 80.27%, H 7.12% $C_{18}H_{20}O_2$ requires C 80.56%, H 7.51%).

4.2.8. (1*R,2*S**,3*R**)-1,2-Bis(4-chloro-phenyl-3-methyl-pent-4-ene-1,2-diol (8b)+(1*R**,2*S**,3*S**)-3-methyl-1,2-bis(4-chloro-phenyl)-pent-4-ene-1,2-diol (9b).** 1.19 g, 71%, light yellow liquid, FAB mass M^+ *m/z* 337, 339, 341 (100:69:1) (M^+); ^1H NMR ($CDCl_3$): δ 0.86 (d, J=6.9 Hz, 3H, $CH_{3\text{-minor}}$), 0.97 (d, J=6.9 Hz, 3H, $CH_{3\text{-major}}$), 1.93 (br s, 1H, exchanges with D_2O), 2.39–2.41 (m, 1H, CH_{minor}), 2.52–2.58 (m, 1H, CH_{major}), 4.61 (d, J=7.5 Hz, 1H, CHPh), 5.02–5.09 (m, 2H, $=CH_2$), 5.78 (ddd, J_1=17.4 Hz, J_2=10.2 Hz, J_3=7.8 Hz, 1H, $=CH_{major}$), 6.05 (ddd, J_1=17.1 Hz, J_2=10.2 Hz, J_3=9 Hz, 1H, $=CH_{minor}$), 7.22–7.32 (m, 6H, ArH), 7.49 (d, J=8.7 Hz, 1H, ArH), 7.92 (d, J=8.7 Hz, 1H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): (major component) δ 13.8 ($CH_{3\text{-major}}$), 44.6 (CH_{major}), 76.5 (CH), 77.2 (C), 115.9 ($CH_{2\text{-major}}$), 127.8 (CH_{major}), 128.5 (CH_{major}), 131.3 (CH_{major}), 132.9 (CH_{major}), 132.3 (CH), 139.9 (CH_{major}), 140.2 (C_{major}), 141.8 (C_{major}), 192.4 (C_{major}). Some signals for minor component are at δ 14.1 ($CH_{3\text{-minor}}$), 46.4 (CH_{minor}), 117.3 ($CH_{2\text{-minor}}$), 128.4 (CH_{minor}), 140.2 (CH_{minor}); IR ν_{max} ($CHCl_3$): 3446 (OH) cm^{-1}. (Found C 63.90%, H 5.00% $C_{18}H_{18}Cl_2O_2$ requires C 64.11%, H 5.38%).

4.2.9. (1*R,2*S**,3*R**)-1,2-Bis(4-methoxy-phenyl)-3-methyl-pent-4-ene-1,2 diol (8c)+(1*R**,2*S**,3*S**)-3-methyl-1,2-bis(4-methoxy-phenyl)-pent-4-ene-1,2 diol (9c).** 1.21 g, 74%, light yellow liquid, FAB mass M^+ *m/z* 328 (M^+); ^1H NMR ($CDCl_3$): δ 0.89 (d, J=6.9 Hz, 3H, $CH_{3\text{-major}}$), 1.01 (d, J=6.6 Hz, 3H, $CH_{3\text{-minor}}$), 1.25 (br s, 2H, 2×OH, exchanges with D_2O), 2.83–2.86 (m, 1H, CH_{major}), 2.90–2.95 (m, 1H, CH_{minor}), 3.73 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 5.19–5.29 (m, 3H, $=CH_2$, CHOH), 5.82 (ddd, J_1=17.4 Hz, J_2=13.4 Hz, J_3=10.5 Hz, 1H, $=CH_{minor}$), 6.11 (ddd, J_1=17.1 Hz, J_2=10.2 Hz, J_3=9 Hz, 1H, $=CH_{major}$), 6.64–6.74 (m, 4H, ArH), 6.96–7.08 (m, 4H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 14.2 ($CH_{3\text{-minor}}$), 16.2 ($CH_{3\text{-major}}$), 44.5 (CH_{minor}), 44.8 (CH_{major}), 55.0 ($OCH_{3\text{-minor}}$), 55.1 ($OCH_{3\text{-major}}$), 76.1 (CH_{minor}), 77.4 (CH_{major}), 80.4 (C_{minor}), 80.6 (C_{major}), 112.4 (CH_{minor}), 112.5 (CH_{major}), 112.8 (CH_{major}), 113.0 (CH_{minor}), 116.2 ($CH_{2\text{-minor}}$), 116.6 ($CH_{2\text{-major}}$), 127.9 (CH_{minor}), 128.1 (CH_{major}), 129.1 (CH_{major}), 129.2 (CH_{minor}), 131.8 (C_{major}), 132.4 (C_{minor}), 132.4 (C_{minor}), 132.5 (CH_{major}), 140.5 (CH_{minor}), 140.1 (CH_{major}), 158.1 (C_{minor}), 158.2 (C_{major}), 158.8 (C_{major}). Signals for major and minor compounds are assigned on the basis of ^1H–^{13}C HETCOR experiment); IR ν_{max} ($CHCl_3$): 3395 (OH), 3440 (OH) cm^{-1}. (Found C 72.85%, H 7.11% $C_{20}H_{24}O_2$ requires C 73.15%, H 7.37%).

4.3. Iodine mediated cyclization of homoallylic alcohols

Procedure B. Sodium hydrogen carbonate (9 mmol) was added to an ice cold solution of homoallylic alcohol (3 mmol) in dry acetonitrile and resulting suspension was stirred for 15 min at 0 °C. Iodine (9 mmol) was added and stirring was continued for 24–72 h at 0 °C in dark (TLC monitoring). The reaction mixture was diluted with water and extracted with $CHCl_3$. The organic layer was washed with saturated aqueous sodium thiosulphate to remove excess of iodine. The organic layer was dried over anhydrous sodium sulphate and was distilled off. The residue was column chromatographed (silica gel 100–200) to isolate substituted tetrahydrofuran derivatives.

4.3.1. (2*R,3*S**,5*R**)-2,3-Diphenyl-3-hydroxy-5-iodomethyl tetrahydrofuran (10).** Procedure B. Higher R_f component: 91 mg, 8%; white solid, mp 98 °C ($CHCl_3$); FAB mass M^+ *m/z* 380; ^1H NMR ($CDCl_3$): δ 1.92 (br s, 1H, exchanges with D_2O), 2.48 (dd, J_1=14.1 Hz, J_2=3.9 Hz, 4-H_b), 2.78 (dd, J_1=14.8 Hz, J_2=9 Hz, 4-H_a), 3.63 (d, J=6.6 Hz, 2H, 5-CH_2I), 4.57–4.72 (m, 1H, 5-H), 5.29 (s, 1H, 2-H), 7.04–7.39 (m, 10H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 10.7 (CH_2I), 48.4 (CH_2-4), 77.9 (CH-5), 82.2 (C-3), 90.8 (CH-2), 125.2 (CH), 126.5 (CH), 127.2 (CH), 128.2 (CH), 128.2 (CH), 134.7 (C), 141.9 (C). NOE experiments: irradiation of singlet at δ 5.29 (2-H) shows positive NOE with signals at δ 4.57–4.72 (5-H), 2.79 (4-H_a) and 7.05, 7.39 (ArH) and irradiation of multiplet at δ 4.57–4.72 (5-H) shows positive NOE with dd at δ 2.79 and doublet at δ 3.63 shows positive NOE with dd at δ 2.48; IR ν_{max} (KBr): 3421 (OH) cm^{-1}. (Found C 53.4%, H 4.2% $C_{17}H_{17}IO_2$ requires C 53.70%, H 4.51%).

4.3.2. (2*R,3*S**,5*S**)-2,3-Diphenyl-5-iodo methyltetrahydro-furan-3-ol (11).** Procedure B. Lower R_f component: 365 mg, 32%; pale yellow liquid; M^+ *m/z* 380 (M^+); ^1H NMR ($CDCl_3$): δ 1.79 (br s, 1H, exchanges with D_2O), 2.45 (dd, J_1=12.9 Hz, J_2=9.3 Hz, 4-H_a), 2.62 (dd, J_1=10.2 Hz, J_2=6.0 Hz, H-4$_b$), 3.49 (dd, J_1=10.2 Hz, J_2=3.3 Hz, 1H of CH_2I), 3.60 (dd, J_1=10.2 Hz, J_2=6.0 Hz, 1H of CH_2I), 4.50–4.59 (m, 1H, H-5), 5.51 (s, 1H, H-2), 6.98–7.45 (m, 10H, ArH); ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 12.4 (CH_2I), 49.4 (CH_2-4), 77.1 (CH-5), 83.4 (C-3), 89.9 (CH-2), 125.3 (CH), 126.6 (CH), 127.4 (CH), 128.3 (CH), 128.4 (CH), 135.1 (C), 141.2 (C). NOE experiments: irradiation of singlet at δ 5.51 (2-H) shows NOE for signals at δ 2.45 (4-H_a) and Ph (δ 7.04, 7.45) but does not show NOE for H-5 (δ 4.50–4.59). The dd at δ 2.62 (H_b) shows positive NOE with signal at H-5 (δ 4.50–4.59); IR ν_{max} ($CHCl_3$): 3546 (OH) cm^{-1}. (Found C 53.4%, H 4.2% $C_{17}H_{17}IO_2$ requires C 53.70%, H 4.51%).

4.3.3. (2*R,3*S**,4*R**,5*S**)-2,3-Diphenyl-4-methyl-5-iodomethyl tetrahydro-furan-3-ol (12a).** Procedure B. 804 mg, 68%, white solid, mp 98 °C ($CHCl_3$); FAB mass M^+ *m/z* 394 (M^+); ^1H NMR ($CDCl_3$): δ 0.91 (d, J=6.9 Hz, 3H, CH_3), 1.61 (br s, 1H, exchanges with D_2O), 2.68 (dq, J_1=9.3 Hz, J_2=6.6 Hz, 1H, CH), 3.48 (dd, J_1=10.8 Hz, J_2=3.3 Hz, 1H, 1H of CH_2I), 3.76 (dd, J_1=10.8 Hz, J_2=3.9 Hz, 1H, 1H of CH_2I), 3.90 (dt, J_1=9.3 Hz, J_2=3.6 Hz, 1H, CH-5), 5.56 (s, 1H, CH-2), 7.02–7.30 (m, 2H, ArH), 7.32–7.47 (m, 8H, ArH); decoupling of dq at δ 2.68 converts doublet at δ 0.91 due to CH_3 into singlet while decoupling of double doublet at δ 3.48 converts double doublet at δ 3.76 into doublet and dt at δ 3.90 into double doublet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 8.7 (CH_3), 12.3 (CH_2), 52.5 (CH), 82.1 (CH), 83.9 (C), 89.5 (CH), 125.6 (CH), 126.6 (CH), 127.4 (CH), 128.3 (CH), 128.3 (CH), 128.4 (CH),

135.4 (C), 140.7 (C). NOE experiments: the irradiation of H-4 dq at δ 2.68 shows NOE with H-2 (7.06%) and CH_2I (3.77, 2.77%). Irradiation of H-5 (δ 3.88–3.93) shows NOE with CH_3 (10.6%) (d, δ 0.92) and irradiation 1H of CH_2I at δ 3.76 shows 16.1% NOE with H-2 and irradiation of other CH_2I proton at δ 3.48 shows 2.8% NOE with H-2 proton at δ 5.56; IR ν_{max} (KBr): 3550 (OH) cm^{-1}. (Found C 54.6%, H 4.6% $C_{18}H_{19}IO_2$ requires C 54.84%, H 4.86%).

4.3.4. (2*R,3*S**,4*S**,5*S**)-2,3-Diphenyl-4-methyl-5-iodomethyl tetrahydro-furan-3-ol (13a).** Procedure B. 590 mg, 5%; pale yellow liquid; FAB mass M^+ *m/z* 394 (M^+); ^1H NMR ($CDCl_3$): δ 0.78 (d, $J=7.5$ Hz, 3H, CH_3), 1.64 (br s, 1H, OH exchanges with D_2O), 2.52 (dq, $J_1=7.5$ Hz, $J_2=4.5$ Hz, 1H, CH-4), 3.15 (t, $J=9.3$ Hz, 1H, 1H of CH_2I), 3.44 (dd, $J_1=9.3$ Hz, $J_2=6.3$ Hz, 1H, 1H of CH_2I), 5.10 (ddd, $J_1=9.0$ Hz, $J_2=6.0$ Hz, $J_3=4.5$ Hz, 1H, CH-5), 5.93 (s, 1H, CH), 7.02–7.30 (m, 2H, ArH), 7.32–7.47 (m, 8H, ArH); decoupling of dq at δ 2.52 converts doublet at δ 0.78 due to CH_3 into singlet while decoupling of triplet at δ 3.15 converts dd at δ 3.44 into doublet and ddd at δ 5.10 into dd. Decoupling of ddd at δ 5.10 converts dd (δ 3.44) and triplet (3.15) into doublets and dq at δ 2.52 into a quartet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 3.8 (CH_2), 10.2 (CH_3), 48.7 (CH), 82.3 (CH), 83.8 (CH), 86.3 (C), 126.9 (CH), 127.2 (CH), 127.7 (CH), 128.1 (CH), 128.2 (CH), 128.4 (CH), 136.8 (C), 140.5 (C). NOE experiments: the irradiation of CH_3 (d, δ 0.78) shows 2.6% NOE enhancement of H-2 (s, δ 5.93) and 2.1% enhancement of 1H of CH_2I (t, δ 3.15). The irradiation of H-4 (dq, δ 2.52) shows 11% NOE enhancement of H-5 (ddd, δ 5.10). Irradiation of H-2 singlet at δ 5.93 shows 2.5% NOE enhancement of 1H of CH_2I (dd, δ 3.44); IR ν_{max} ($CHCl_3$): 3495 (OH) cm^{-1}. (Found C 54.34%, H 4.70% $C_{18}H_{19}IO_2$ requires C 54.84%, H 4.86%).

4.3.5. (2*R,3*S**,4*R**,5*S**)-2,3-Bis(4-chlorophenyl)-4-methyl-5-iodomethyltetrahydrofuran-3-ol (12b).** Procedure B. 930 mg, 68%, white solid, mp 120 °C ($CHCl_3$); FAB mass M^+ *m/z* 463 (M^+); ^1H NMR ($CDCl_3$): δ 0.90 (d, $J=6.9$ Hz, 3H, CH_3), 1.49 (br s, 1H, exchanges with D_2O), 2.63 (dq, $J_1=9$ Hz, $J_2=6.9$, 1H, CH-4), 3.47 (dd, $J_1=10.8$ Hz, $J_2=3.3$ Hz, 1H, 1H of CH_2I), 3.75 (dd, $J_1=10.8$ Hz, $J_2=3.6$ Hz, 1H, 1H of CH_2I), 3.86 (dt, $J_1=9.3$ Hz, $J_2=3.6$ Hz, 1H, CH-5), 5.46 (s, 1H, CH-2), 6.94–6.98 (m, 2H, ArH), 7.20–7.26 (m, 2H, ArH), 7.32–7.38 (m, 8H, ArH); decoupling of dq at δ 2.63 converts doublet at δ 0.90 due to CH_3 into singlet and double triplet at δ 3.86 into singlet while decoupling of dd at δ 3.47 converts double doublet at δ 3.75 into doublet and dt at δ 3.86 into triplet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 8.6 (CH_3), 12.0 (CH_2), 52.3 (CH), 81.9 (CH), 83.6 (C), 88.8 (CH), 127.0 (CH), 127.9 (CH), 128.5 (CH), 128.7 (CH), 133.5 (CH), 133.7 (CH), 134.2 (C), 138.9 (C). NOE experiments: the irradiation of H-2 singlet at δ 5.46 shows 6.03% NOE with H-4 (δ 2.63); irradiation of CH_3 doublet at δ 0.90 shows 2.5% NOE with H-5 (δ 3.86) and irradiation of one of CH_2I proton at δ 3.47 shows 4% NOE with H-4; IR ν_{max} (KBr): 3529 (OH) cm^{-1}. (Found C 47.00%, H 3.20% $C_{18}H_{17}Cl_2IO_2$ requires C 46.68%, H 3.70%).

4.3.6. (2*R,3*S**,4*S**,5*S**)-2,3-Bis(4-chlorophenyl)-4-methyl-5-iodomethyltetrahydro-furan-3-ol (13b).** Procedure B. 70 mg, 5%; pale yellow liquid; FAB mass M^+ *m/z* 463 (M^+); ^1H NMR ($CDCl_3$): δ 0.79 (d, $J=7.5$ Hz, 3H, CH_3), 1.64 (br s, 1H, OH exchanges with D_2O), 2.49 (dq, $J_1=7.5$ Hz, $J_2=4.5$ Hz, 1H, CH-4), 3.13 (t, $J=9.3$ Hz, 1H, 1H of CH_2I), 3.42 (dd, $J_1=9.9$ Hz, $J_2=6.3$ Hz, 1H, 1H of CH_2I), 5.07 (ddd, $J_1=9.0$ Hz, $J_2=5.4$ Hz, $J_3=4.5$ Hz, 1H, CH-5), 5.81 (s, 1H, CH), 7.03–7.50 (m, 10H, ArH); decoupling of dq at δ 2.49 converts doublet at δ 0.79 due to CH_3 into singlet and ddd at δ 5.07 into a dd, while decoupling of ddd at δ 5.07 converts dd at δ 3.42 and triplet at δ 3.13 into two doublets and dq at δ 2.49 into quartet; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): δ 3.4 (CH_2), 10.2 (CH_3), 48.7 (CH), 82.5 (CH), 83.3 (CH), 86.0 (C), 128.3 (CH), 128.4 (CH), 128.6 (CH), 128.7 (CH), 133.9 (C), 134.1 (C), 135.1 (C), 138.8 (C). NOE experiments: the irradiation of CH_3 (d, δ 0.79) shows 3.62% NOE enhancement of H-2 (s, δ 5.81) and 3.36% enhancement of 1H of CH_2I (t, δ 3.13). The irradiation of H-4 (ddd, δ 2.49) shows 13.06% NOE enhancement of H-5 (ddd, δ 5.07); IR ν_{max} ($CHCl_3$): 3436 (OH) cm^{-1}. (Found C 47.05%, H 3.26% $C_{18}H_{17}Cl_2I\ O_2$ requires C 46.68%, H 3.70%).

4.3.7. (2*R,3*S**,4*S**,5*S**)-2,3,4-Triphenyl-5-iodomethyl tetrahydro-furan-3-ol (14a) (2*R**,3*S**,4*S**,5*R**)-2,3,4-triphenyl-5-iodomethyltetrahydro-furan-3-ol (15a).** Procedure B. 1.1 g, (81%), transparent liquid, FAB mass M^+ *m/z* 456 (M^+); ^1H NMR ($CDCl_3$): (major) (**14a**): δ 1.79 (br s, 1H, OH exchanges with D_2O), 3.19 (dd, $J_1=9.6$ Hz, $J_2=8$ Hz, 1H, 1H of CH_2I), 3.51 (dd, $J_1=9.6$ Hz, $J_2=6.9$ Hz, 1H, 1H of CH_2I), 3.64 (d, $J=4.5$ Hz, 1H, H-4), 5.46 (ddd, $J_1=7.2$ Hz, $J_2=6.9$ Hz, $J_3=4.5$ Hz, 1H, H-5), 6.11 (s, 1H, CH-2), 6.95–7.26 (m, 15H, ArH $_{(major+minor)}$). Compound **15a** (minor): δ 1.84 (br s, 1H, OH exchanges with D_2O), 3.61 (d, $J=3.9$ Hz, 1H, H-4), 3.82 (d, $J_1=6.6$ Hz, 2H, CH_2I), 4.87 (dt, $J_1=6.6$ Hz, $J_2=3.9$ Hz, 1H, H-5), 5.87 (s, 1H, CH-2). Decoupling of dt at δ 4.87 due to minor component converts doublet at δ 3.82 and 3.61 into singlet. Decoupling of 1H ddd at δ 5.46 (H-5 major diastereomer) converts H-4 doublet (δ 3.64) into singlet and two dds of CH_2I (δ 3.19 and 3.51) into two doublets; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): (compound **14a** major) δ 4.2 (CH_2), 63.2 (CH), 83.1 (CH), 85.2 (CH), 86.3 (C), 126.4 −139.8 (CH). Compound **15a** (minor) δ 10.5 (CH_2), 63.7 (CH), 84.3 (CH), 86.6 (CH), 86.8 (C). ^{13}C NMR signals have been assigned on the basis of ^1H–^{13}C HETCOR experiment. NOE experiments: in major diastereomer, irradiation of H-5 (ddd, δ 5.46) shows NOE with H-4 (14.2%, δ 3.63) and irradiation of H-2 (s, δ 6.11) shows NOE with 1H of CH_2I (9.17%, δ 3.51). In minor isomer, irradiation of H-5 (dt, δ 4.87) shows NOE with H-2 (4.76%, δ 5.87) and irradiation of CH_2I (d, δ 3.82) shows NOE with CH-4 (5.34%, δ 3.61). IR_{major} ν_{max} ($CHCl_3$): 3535 (OH) cm^{-1}. (Found C 59.89%, H 4.92% $C_{23}H_{21}IO_2$ requires C 60.54%, H 4.64%).

4.3.8. (2*R,3*S**,4*S**,5*S**)-2,3-Bis(4-chloro-phenyl)-5-iodo methyl-4-phenyl-tetrahydro-furan-3-ol (14b) (2*R**, 3*S**,4*S**,5*R**)-2,3,4-triphenyl-5-iodomethyltetrahydro-furan-3-ol (15b).** Procedure B. 1.05 g, (81%), transparent liquid, FAB mass M^+ *m/z* 525 (M^+); ^1H NMR ($CDCl_3$): (major) (**14b**): δ 1.72 (br s, 1H, OH exchanges with D_2O), 3.18 (dd, $J_1=9.9$ Hz, $J_2=8.4$ Hz, 1H, 1H of CH_2I), 3.49 (dd, $J_1=9.6$ Hz, $J_2=7.2$ Hz, 1H, 1H of CH_2I), 3.60 (t, $J=$

3.9 Hz, 1H, H-4), 5.42 (ddd, $J_1=8.1$ Hz, $J_2=6.6$ Hz, $J_3=4.5$ Hz, 1H, H-5), 5.97 (s, 1H, CH-2), 7.02 (m, 13H, ArH $_{(major+minor)}$). Compound **15** (minor): δ 1.72 (br s, 1H, OH exchanges with D_2O), 3.49 (t, $J=3.9$ Hz, 1H, H-4), 3.77 (d, $J=6.6$ Hz, 2H,CH_2I), 4.84 (ddd, $J_1=6.6$ Hz, $J_2=6.6$ Hz, $J_3=3.3$ Hz, 1H, H-5), 5.73 (s, 1H, CH-2). In minor component, decoupling of ddd at δ 4.84 converts doublet at δ 3.77 into singlet and triplet at δ 3.59 into distorted triplet. While decoupling of 1H ddd at δ 5.42 (H-5 major diastereomer) converts triplet at δ 3.59 (H-4) into singlet and two dds at δ 3.175 and 3.49 (CH_2I) into two doublets; ^{13}C NMR (normal/DEPT-135) ($CDCl_3$): (compound 14 major) δ 3.6 (CH_2), 63.0 (CH), 83.3 (CH), 84.9 (CH), 86.1 (C), 127.3–138.2 (CH, C)$_{major+minor}$ (compound **15b** minor) δ 10.0 (CH_2), 63.6 (CH), 84.3 (CH), 86.0 (CH), 86.5 (C). In major diastereomer, irradiation of H-5 (ddd, δ 5.42) shows 14% NOE enhancement of H-4 (δ 3.59) and irradiation of H-2 (s, δ 5.97) shows 3.86% NOE enhancement with 1H of CH_2I (δ 3.49). In minor diastereomer, irradiation of H-5 (ddd) shows 2.31% NOE enhancement of H-2 (δ 5.73) and irradiation of CH_2I doublet (δ 3.77) shows 5.17% NOE enhancement of CH-4 (δ 3.59). IR$_{major}$ ν_{max} ($CHCl_3$): 3544 (OH) cm^{-1}. (Found C 53.01%, H 3.98% $C_{23}H_{19}Cl_2IO_2$ requires C 52.60%, H 3.65%).

4.4. X-ray crystal data collection for 12b

X-ray crystal data was measured by using θ–2θ scan mode. The structures were solved by using direct method SHELX-97. CCDC 284604, molecular formulae $C_{18}H_{17}IO_2$; triclinic space group P-1, $a=9.0434$ Å, $b=10.3870$ Å, $c=11.0240$ Å, $\alpha=78.543(4)°$, $\beta=84.009(5)°$, $\gamma=66.497(6)°$, $V=930.33(10)$ Å^3, $Z=2$, $D_c=1.653$ mg/m^3, θ range for data collection 1.89–24.97°. The structure solution is based on 3453 reflections, which converged to $R=0.0150$. Refinement method: full-matrix least squares on $F2$, goodness of fit=1.058.

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